GENES, MEDICINE, AND THE NEW RACE DEBATE

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JUNE 2003

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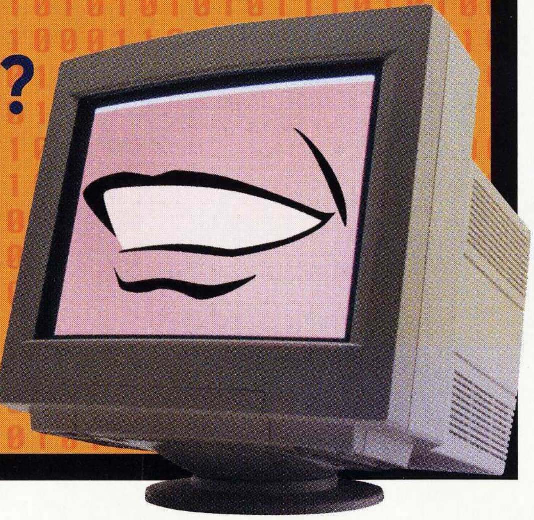

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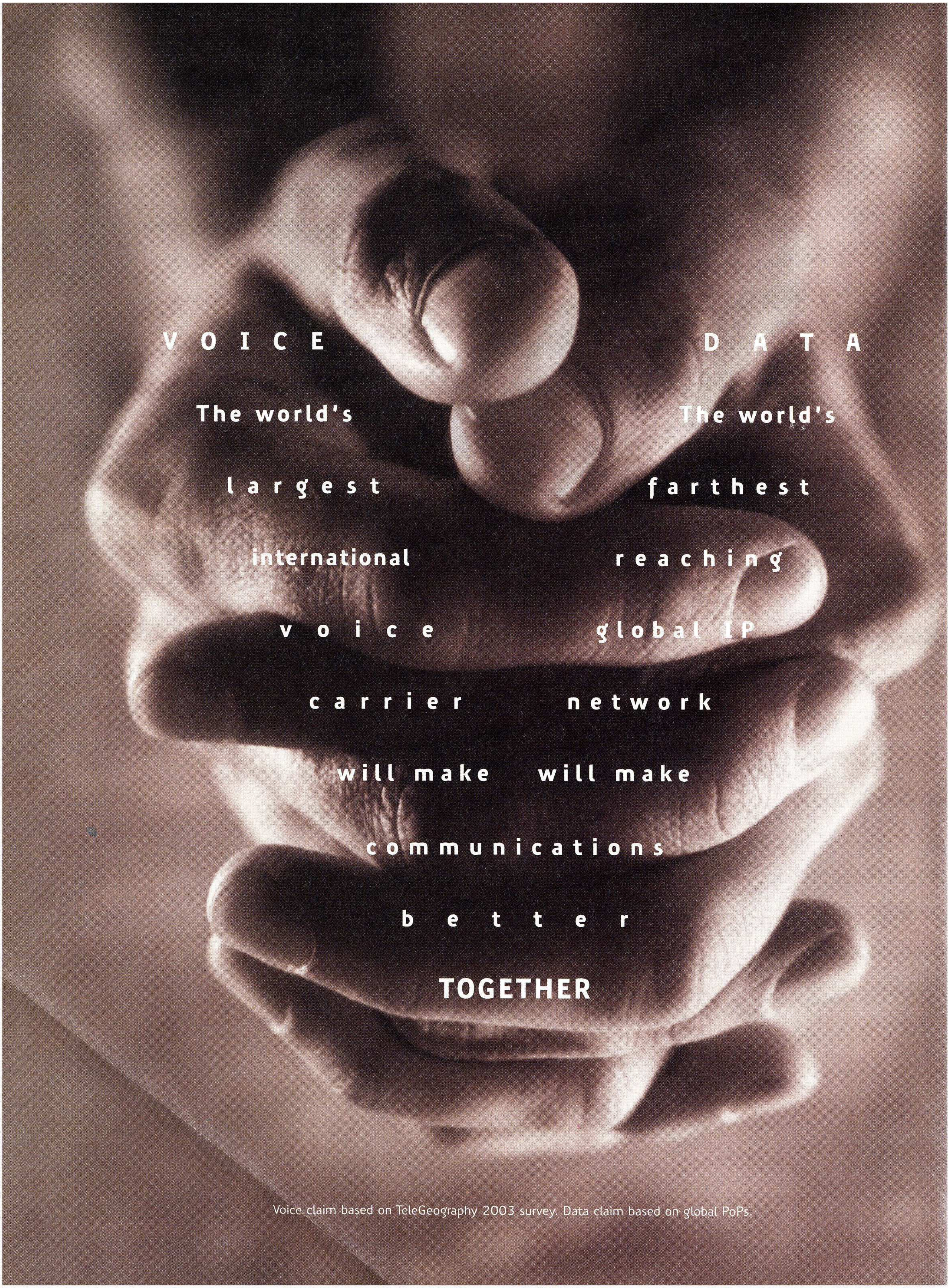
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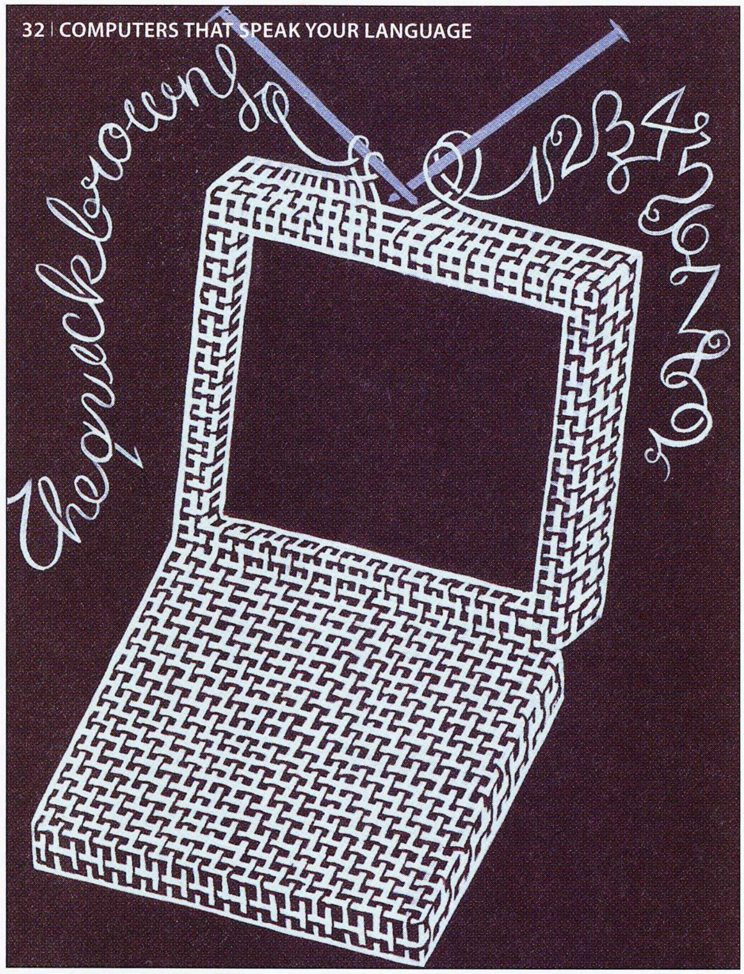
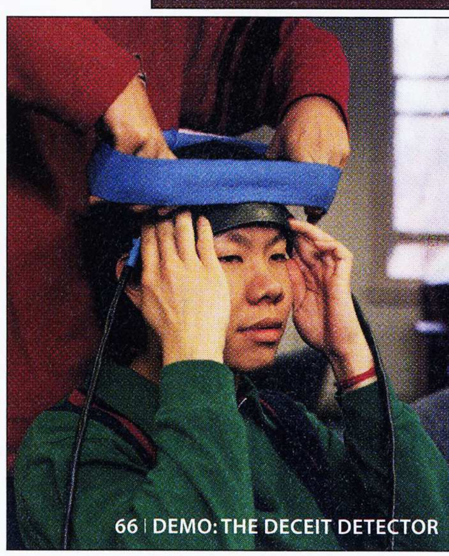
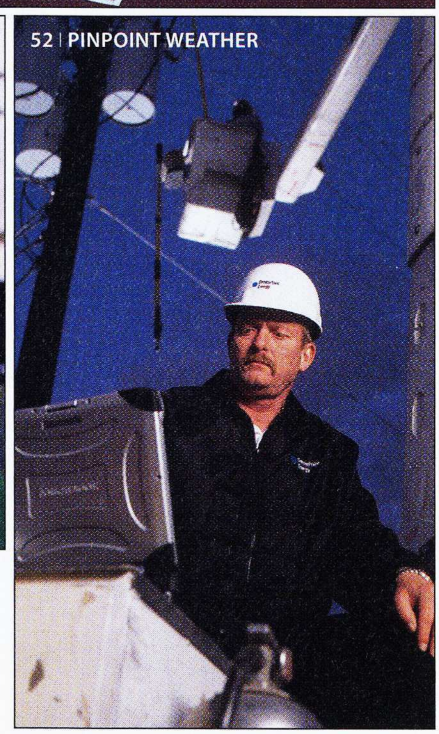
CONTENTS

TECHNOLOGY REVIEW VOLUME 106, NUMBER 5

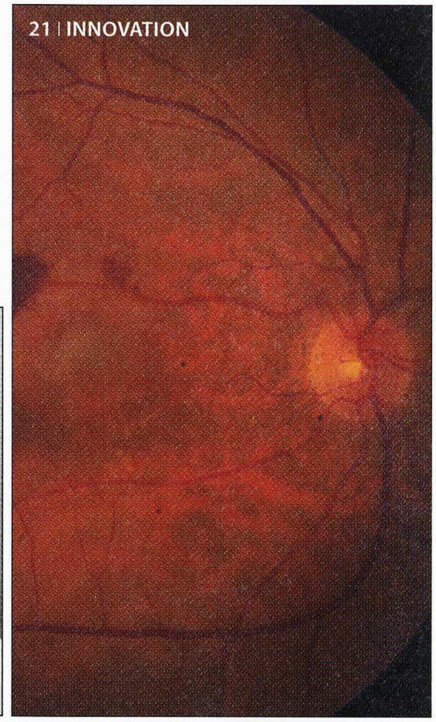

32 | COMPUTERS THAT SPEAK YOUR LANGUAGE


66 | DEMO: THE DECEIT DETECTOR

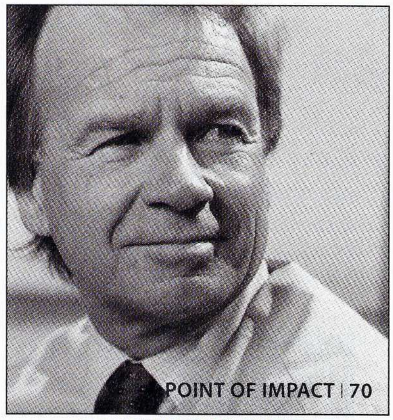

52 | PINPOINT WEATHER

DEPARTMENTS

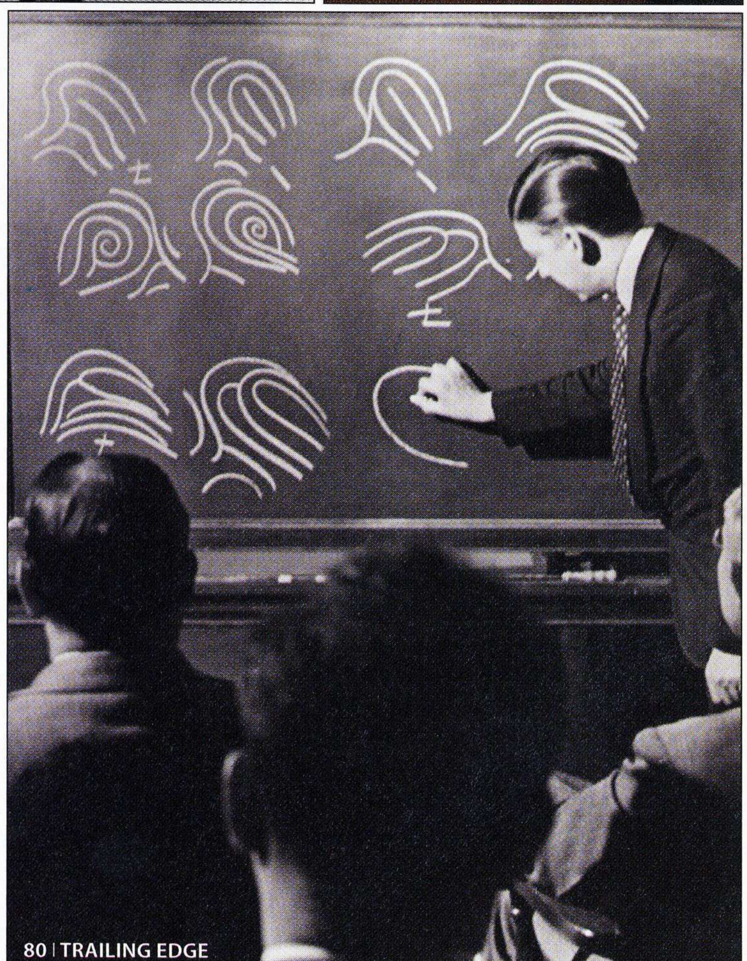
COLUMNS



21 | INNOVATION



POINT OF IMPACT | 70



80 | TRAILING EDGE

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AN MIT ENTERPRISE TECHNOLOGY REVIEW

LEADING EDGE

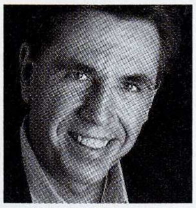
FROM THE EDITOR IN CHIEF

VIVE LA DIFFERENCE

Walk down a crowded street in just about any major U.S. city (and many others around the world) and you will encounter people who speak a panoply of languages and whose skin colors span a broad range of tones. Depending on where you live and work, you might enjoy the same rich mosaic in your neighborhood, office, and schools. We celebrate such diversity, because it opens people's minds to different cultures and works to break down barriers of distrust and ignorance that too often divide people of varying backgrounds.

But contemporary society's embrace of diversity comes with an element of caution and even discomfort. Especially with issues that touch upon race, we seem reluctant to probe too closely—in both the social and scientific spheres. The revolution in genomics, however, which is describing our DNA in exacting detail, is almost forcing scientists to confront differences between the world's population groups. And not being afraid to ask potentially controversial questions about our differences is what makes this issue's article "Genes, Medicine, and the New Race Debate" *(p. 40)* so compelling.

Written by *TR* executive editor David Rotman, it's the story of a $100 million effort called the International HapMap Project. A natural extension of the Human Genome Project, which produced a master copy of the human DNA sequence, the HapMap Project aims to identify common variations in people's DNA that seem to act as signposts for such debilitating diseases as diabetes, hypertension, and schizophrenia. If successful, the project will make it possible to assess an individual's risk factors for these diseases as well as identify the drugs that will likely work for him or her.



But here's the catch. In order for the HapMap to be truly relevant to people everywhere, it will have to spell out in great detail the genetic variations between people from different regions of the world. And bioethicists, sociologists, and other scientists are rightfully concerned that this genetic information could, as our story states, "be manipulated to give an air of biological credence to ethnic stereotypes, to revive discredited racial classifications, and to fuel bogus claims of fundamental genetic differences between groups."

The HapMap researchers are walking a tightrope. The project will almost inevitably find some genetic differences between population groups: this is part of the diversity we celebrate. It's valuable, even vital, to explore these differences, so long as we do so without reverting to old racial or ethnic stereotypes.

The HapMap effort is showing encouraging sensitivity on this point. Before even embarking on this quest, organizers formed the Population and Ethical, Legal, and Social Implications Group. Consisting of 19 well-known social scientists and genomics researchers, the group worked hard to ensure the project was conducted in an open fashion, with donors fully understanding the issues behind it (HapMap information will be publicly available on the Web). "From the very beginning, there's been a lot of concern that this be done in as good a way as is possible," says Ellen Wright Clayton, director of Vanderbilt University's Genetics and Health Policy Center and cochair of the ethics group. Now, she says, as the project expands, the group is being reconfigured to become even more international and reflective of the people it touches.

The HapMap project is of immense potential benefit to people of all backgrounds. So long as investigators go forward as responsibly as they have begun, society has nothing to fear from what it reveals. —*Robert Buderi*

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TECHNOLOGY REVIEW

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LETTERS

INSIGHTS AND OPINIONS FROM OUR READERS

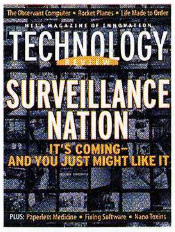
SURVEILLANCE NATION

In "Surveillance Nation" (*TR* April 2003), Dan Farmer and Charles C. Mann write this chilling sentence: "But the rise of omnipresent surveillance will be driven as much by ordinary citizens' understandable—even laudable—desires for security, control, and comfort as by the imperatives of business and government." It is understandable, yes; but in what sense is it laudable?

Daniel Stroock
Cambridge, MA

ROCKET PLANES

The aerospace industry ("Countdown for Rocket Planes, *TR* April 2003) must convince the public that it represents a resource to be strengthened and not a profit-grabbing industry that diverts national resources from more important endeavors. While the industry possesses advanced technology resources to help solve many of our social and civil problems, this is only part of what must continue to be a balanced application of science and technology. If this balance is to be achieved, the ingenious aerospace chiefs have to find ways to direct more of their skills to down-to-earth problems, and the government will have to scratch up more resources to retain their workers. I write as a former insider in this industry: I was a senior scientist at Lockheed Engineering and Management Service.



Aerospace chiefs have to find ways to direct more of their skills to down-to-earth problems, and the government has to scratch up more resources to retain workers.

Jordan C. Fan
Upper Marlboro, MD

PAPERLESS MEDICINE

Electronic medical records would be a godsend, but they have remained impossible to achieve ("Paperless Medicine," *TR* April 2003). First, a doctor needs to sign off on everything that comes in, and information is easier to process on paper than on a computer. Second, paper documents need to be scanned into a system, which is expensive. Ideally, each document would carry a universally formatted tag encoding its identity. However, there are no standard machine-readable markers for documents to code the identity of the patient, the type of document, and its source. Solve these problems, make the system work with accurate freestyle voice recognition, keep the cost down, and the industry will have a winner.

Jeffrey L. Kaufman
Springfield, MA

LIFE MADE TO ORDER

We should be concerned about potential effects of creating new or chimeric organisms using novel, synthetic DNA ("Life Made to Order," *TR* April 2003). We don't want to realize in 50 years that we inadvertently created new classes of compounds that accumulate in the biosphere because no naturally occurring organism can metabolize them. Consider the pesticides that, decades later, turned out to be hormones in most animals, as well as in the insects originally targeted.

Duncan Rhodes
Cerrillos, NM

WRITING SOFTWARE RIGHT

The article "Writing Software Right" (*TR* April 2003) missed the boat. Not once does the article mention the design portion of software creation—the most time- and cost-saving point at which to catch structural bugs. The article ends by quoting a Microsoft employee who suggests that poor software quality is due to a lack of testing tools. This is absolutely incorrect. One can't slap code together willy-nilly, subject it to some testing tools right before a production release (no matter how good the testing tools are), and then expect the code to be bug free while meeting the user's requirements.

Carrie M. Smith
Delaware, OH

BIG IVORY TAKES LICENSE

Columnist Seth Shulman advocates radical changes in the licensing practices of U.S. universities ("Big Ivory Takes License," *TR* April 2003). He compares the license income of academia with that of IBM, praises the fact that IBM primarily licenses nonexclusively, and based on a single lawsuit concludes that universities shouldn't grant exclusive licenses on the patents they create. Shulman ignores the fact that his approach was tried for 30 years—and didn't work. Only since the passage of the Bayh-Dole Act in 1980 have universities been free to license their patents on terms appropriate to each invention. New industries have been built on academic research. Let's not return to the dark ages.

Ashley J. Stevens
Director, Office of Technology Transfer
Boston University
Boston, MA

Correction: In the April 2003 article "Surveillance Nation," we misstated the relationship between exabytes and gigabytes. In fact, 200 exabytes equals 200 billion gigabytes.

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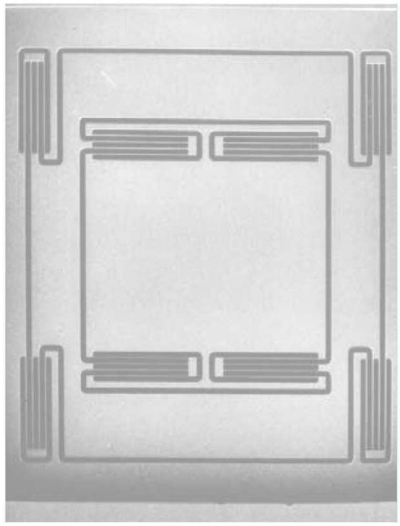
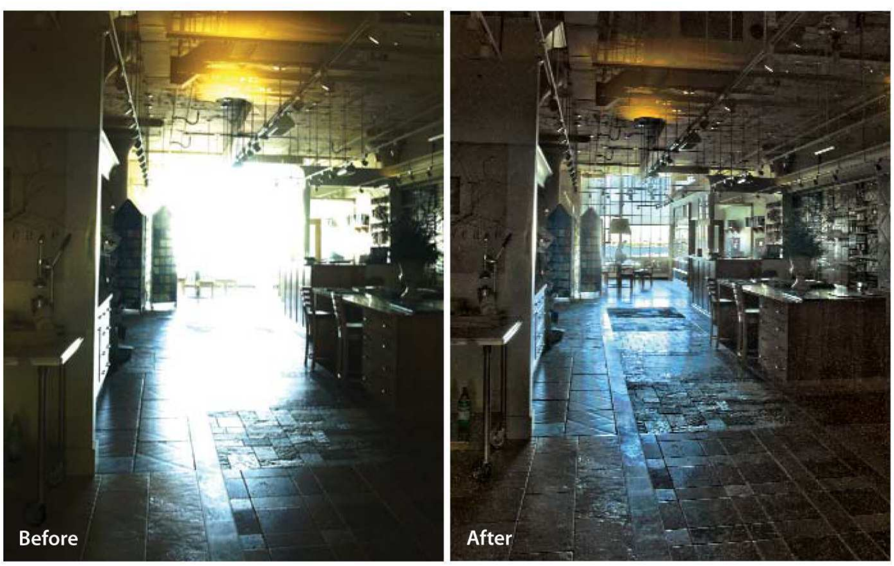
MICRO-MOVER

A tiny motorized table that is able to slide sideways in increments measured in atom-widths could offer a way to vastly increase computers' memory capacity. The "micro-mover," as it's called by its inventors at Agilent Laboratories in Palo Alto, CA, is carved into a silicon chip three millimeters wide. The mover sits on two sets of flexible legs that bend slightly under electrostatic forces; one set flexes in the north-south direction, the other east-west. In this way, the device can skate to any of a billion positions in increments of five nanometers—about the width of a dozen atoms, says Farid Matta, manager of the group that built the device. Researchers have long envisioned memory devices that would pack bits as closely as individual molecules in a solid material, but any such storage device requires "something that moves under the read-write tool to allow you to write a one or a zero in a new spot," Matta explains. The micro-mover is sprightly and precise enough to do that with individual molecules, he says—potentially writing up to 125 megabytes of data in an area only 50 micrometers on a side.



Agilent's silicon positioning device slides in 1.5-nanometer increments.



PICTURE PERFECT

Even Ansel Adams struggled with light, employing tricky developing techniques to preserve detail and avoid large areas of a print appearing washed out or too dark. Now, amateur photographers can produce artfully balanced images with a new digital-processing algorithm.

Developed by MIT computer scientist Frédo Durand, the process reduces excessive contrast in the picture without losing detail and takes only a couple of seconds. It starts with a digitized image, either from a digital camera or a scan of a negative, and partitions the image data in unique ways. The first partition is into color (which the algorithm does not touch) and light-intensity components. The computer next subdivides the intensity component into one comprising the picture's details and one containing a map of large-scale variations in luminosity. The algorithm then reduces the variations in this final component. Durand hopes the technology will first be employed in software that digital photographers use to download their pictures from camera to computer, which could transform those vacation snapshots from awful to art.

FLAT-SCREEN 3-D

Father and son inventors Paul and Ilan Kleinberger have developed a flat-screen 3-D display that eliminates the flicker, low resolution, and bulky glasses that detract from other 3-D methods. 3-D effects are created by showing slightly different images to each eye. At startup 3ality in Jerusalem, Israel, the Kleinbergers use their own software to combine left- and right-eye image data so that each pixel on a liquid-crystal display contains the information for both eyes. 3ality adds an extra liquid-crystal layer that "twists" the resulting light, giving a different polarization to each eye's image. That way, a viewer wearing lightweight polarizing glasses gets an uninterrupted, full-resolution image for each eye. 3ality has built prototypes in cooperation with the U.S. Army; company president Yosh Mantinband says the displays should be ready to market by 2005.

BUILDING BROWSER

Imagine walking down the street and browsing the contents of a store by pointing a handheld computer at it. Up pops a list of available products and services, and even comments from customers. At Hewlett-Packard Laboratories in Palo Alto, CA, engineer Salil Pradhan's team has developed such a mobile interface. The software runs on a personal digital assistant or cell phone, automatically linking to Web sites associated with nearby buildings. Unlike tracking systems that use bar codes or radio frequency ID tags, Pradhan's device works at distances greater than 10 meters; it calculates the user's position and orientation using a Global Positioning System receiver and a digital compass embedded in the handheld. Pradhan is expanding the system to work indoors. A product could be available in three years, he says.

Hewlett-Packard's point-and-shop software.

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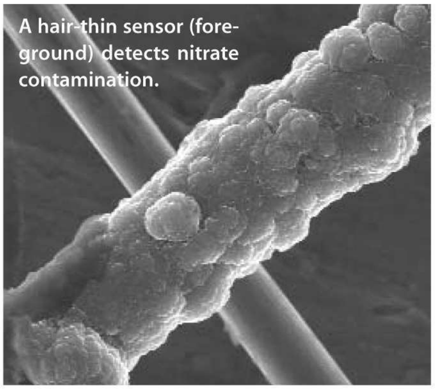


A hair-thin sensor (foreground) detects nitrate contamination.

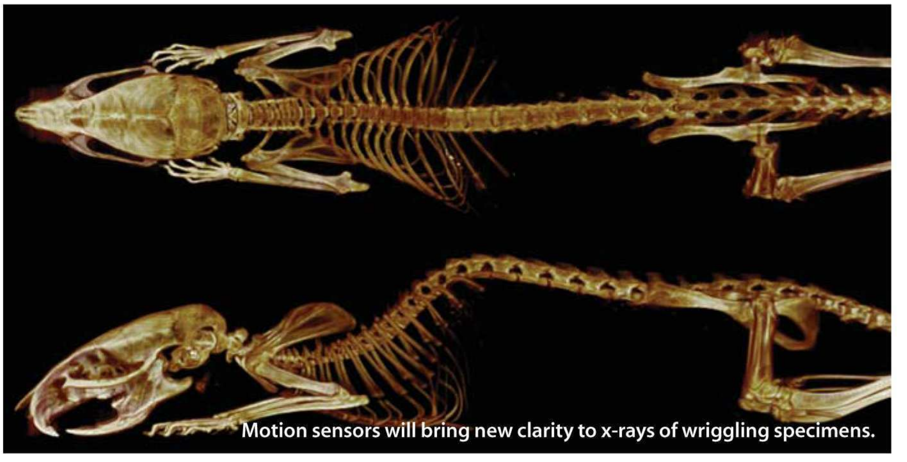
SAFER SOIL

Off-the-shelf devices that detect contaminants are bulky and expensive and require frequent recalibration. At the University of California, Los Angeles, engineers Tom Harmon and Jack Judy have built a tiny sensor that could improve soil monitoring of nitrates, which can leak into ground water and cause health problems. The sensor consists of a carbon rod coated with a mix of polymer and nitrate. Placing it in water or moist soil generates a voltage that corresponds to the difference between the nitrate concentrations of the soil and the coating.

The hair-thin, 1.5-centimeter-long device could be mass-produced on silicon chips, says Harmon, lowering the cost to one-tenth that of conventional nitrate detectors. Eventually, the sensor will self-calibrate based on models of how environmental factors, such as temperature, affect the signal. In five years, Harmon says, the effort could yield arrays of cheap, reliable sensors that need little human intervention once deployed.

DATA-MINING DRIVES

You want to find that digital shot of your belly-flopping husband from last summer's vacation, but you can't remember where you filed it on your hard drive. What if, rather than making you open folder after folder, your hard drive acted more like a database, quickly serving up the file you want? That's the idea behind a project in Mahadev Satyanarayanan's Intel-sponsored lab at Carnegie Mellon University to create software for special processors inside hard drives. The software would speed searches by examining hard-drive data as they're read and suppressing all the data that have no chance of fitting the search parameters before they reach a computer's main processor. If assigned to look for a suspected terrorist in video surveillance data, for example, the system could block frames showing empty sidewalks. If intelligence officers, radiologists, astronomers, or other professionals who depend on data from images express interest in the group's early simulations, then Intel could start working with them within a year or two to build specialized hard-drive software, and eventually hardware, Satyanarayanan says.



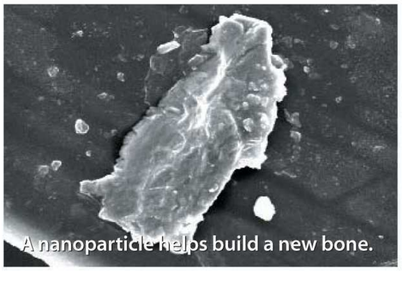
Motion sensors will bring new clarity to x-rays of wriggling specimens.

SQUIRM SCAN

Making brain scans of children and of people with conditions like Parkinson's disease is difficult because the patients have trouble keeping still. Soon, though, technology initially designed to let geneticists scan even-squirmier patients—mice—just might help. Being developed jointly at Oak Ridge National Laboratory in Tennessee and the Thomas Jefferson National Accelerator Lab Facility in Newport News, VA, the system tracks—and compensates for—patient movement during a scan. Reflective markers are attached to the head; an infrared strobe light illuminates these markers, and two infrared cameras monitor the reflections. The position data derived from these cameras are then used to correct the scan information by determining where an x-ray, in the case of a single-photon emission tomography scan, would have hit the detector had the head not moved. Sorting out the data allows the researchers to deliver a crisp, accurate image. Tests of the technology began on mice in March, and the team hopes a fully functional version will be helping humans in two to three years.

ALUMINUM BONE

Tissue engineers have made great strides in growing bone parts in the lab, but it is proving much more difficult to replace whole sections of leg or arm bones, which sustain constant pounding. Researchers at Rice University have developed a technique for growing bone tissue strong enough to withstand the stresses of everyday activity. Conventional bone-tissue engineering involves replacing lost bone with a biodegradable polymer scaffold seeded with cells. As the polymer degrades, new tissue develops. But in load-bearing parts of the skeleton, cells are constantly breaking down and forming new bone in response to mechanical stimuli. If the polymer scaffold placed in a patient's leg is too weak, the material falls apart under this stress. To reinforce their scaffold material, Rice bioengineer Antonios Mikos and chemist Andrew Barron added nanoparticles of alumoxane (an aluminum-based compound) to a photosensitive polymer. Shining light on this blend spurs the nanoparticles to fix themselves to the polymer chains. The resulting material's compressive strength is three times that of the polymer alone. Mikos hopes to start testing the material in rabbits this summer.



A nanoparticle helps build a new bone.

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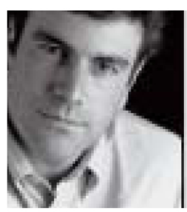
AMATEUR INNOVATION

Historically, household robotics have made for fabulous science fiction but miserable business ventures. Even chronically ingenious entrepreneurs like Atari's Nolan Bushnell and the British innovator James Dyson of vacuum cleaner fame found that their robot ventures did a better job of capturing imaginations than customers. And with the notable exception of Sony's cute but useless Aibo robo-dog, technology's giants have all steered clear of the mass-market robot. No "General Robotics" here.

Yet MIT artificial-intelligence guru Rodney Brooks, cofounder of the Asimov-inspired startup iRobot, seems oddly optimistic about the prospect of robotics. His reason? The technology has finally acquired that vital human ingredient that has made a number of similar industries possible: hobbyists and enthusiasts. "Over 20 years ago, people who liked new technologies played with PCs," says Brooks. "Now they're playing with robots. The first PCs couldn't do very much, and neither can the first generation of robots. But they get people interested and excited."



The same types of students and enthusiasts who once built Heathkits and Altairs—or rebuilt Packards and Nash Ramblers—are taking bots seriously. Bot books, publications, and kits that once sold in the thousands now sell in the tens of thousands. Popular television shows like *BattleBots* and *Junkyard Wars* have brought the essence of MIT's famed Electrical Engineering 270 competition, where students design and build dueling bots, to mainstream awareness. Homebuilt robotics is still more cult than subculture, but its growing popularity is raising a multibillion-dollar business question: will hobbyist/enthusiasts once again be the vanguard of a global industry that matters?

Peel the hagiographic gloss off heroic inventors and you find hobbyists and enthusiasts consistently playing a critical role in the design and diffusion of innovation. So-called home-brew computing made U.S. leadership in personal computing possible. Photography has from its very beginnings been a technology where amateurs exert a greater influence on product development than professionals. The earliest days of radio featured homemade "cats' whiskers" and germanium crystal receivers. Henry Ford may have started making cars on assembly lines, but automobile innovations have been driven as much by hot-rodders and enthusiasts as industry engineers. Aviation's origins similarly feature do-it-yourself aerophiles whose passion for airplanes created levels of public awareness and participation that helped launch the industry. The open-source-software movement, under the leadership of Linus Torvalds and Richard Stallman, also reflects a strong hobbyist/enthusiast ethos.

These amateurs enjoy a special niche in the ecology of innovation because they are simultaneously both creators and consumers; they adapt and adopt. They're not (initially, at least) driven by money; they innovate out of curiosity and pride and necessity. They like to prototype and play. Many of them care far more about cleverness and creativity than the technologies' original inventors. Indeed, Intel's former CEO Andy Grove has publicly acknowledged that he completely missed how important personal computing would become and dismissed PC hobbyists as little more than fanatics. In fact, computer enthusiasts not only reframed the market as consumers but provided vital innovation and served as ardent evangelists for the cause.

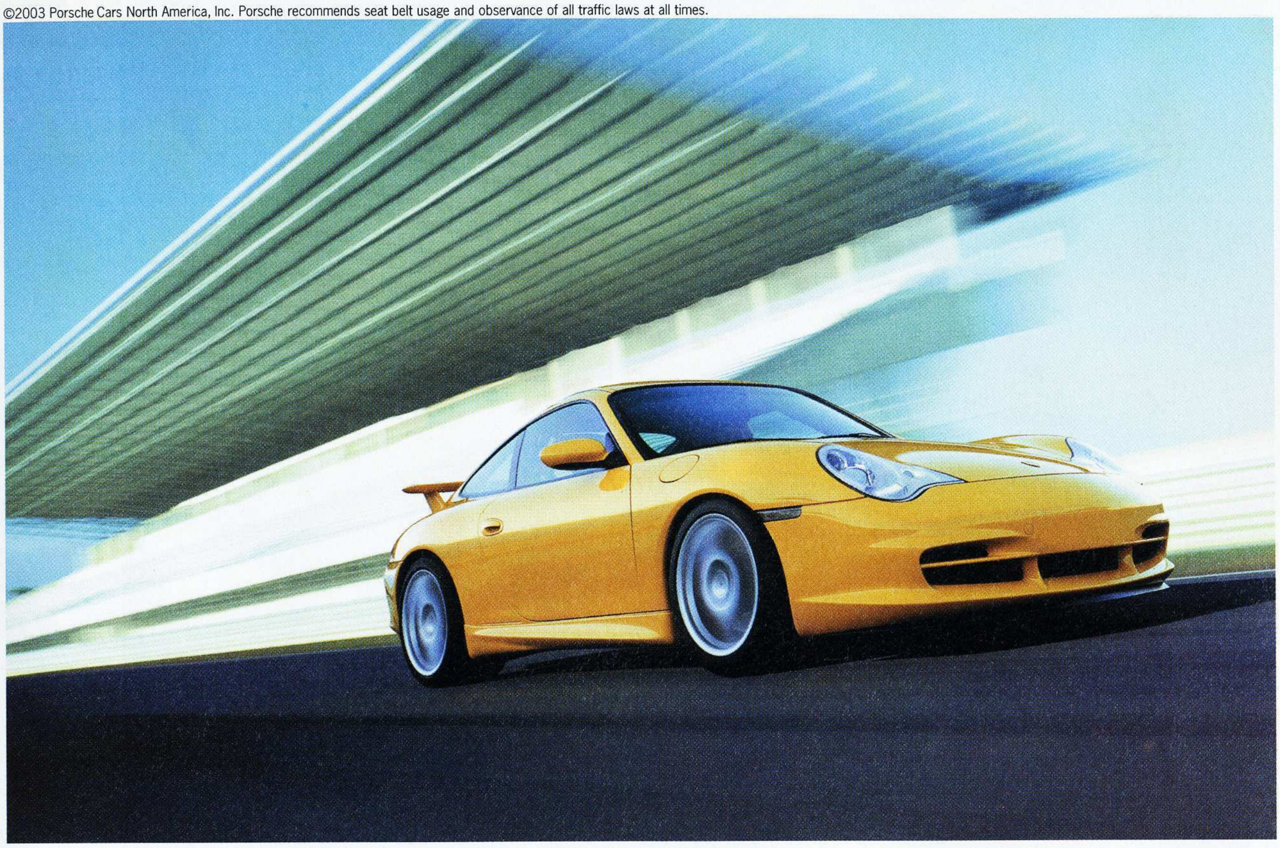
Of course, there's a limit to what enthusiasts can accomplish on their own. "Generally speaking, hobbyists are not able to push forward the boundaries of technology," concedes Dyson. "As soon as any real innovative steps forward are made, the hobby becomes expensive, and hobbyists may have to turn professional to pursue their ideas."

Peel off the hagiographic gloss and you find hobbyists and enthusiasts playing a critical role in the design and diffusion of innovation. Perhaps this decade will bring a Bill Gates of bio-hackerdom.

Still, the essential point remains that innovative firms frequently gain their keenest insights from innovative customers. Those customers often prove to be their most ardent hobbyist/enthusiasts. (Surely, Bill Gates was the most profitable hobbyist Intel could have ever hoped to meet—for better or worse.) This is a phenomenon that companies who are intent on tinker-proofing their products ignore at their peril *(see "You Bought It. Who Controls It?" p. 60)*.

Robotics is hardly the only emergent industry that can expect the embrace of the techno-enthusiast. Maybe bathtub biotech will be next to capture the mindshare of the techie tinkerers. Maybe bioinformatics and the diffusion of genetic engineering technologies and techniques will inspire a new generation of bio-hackers. Certainly the technologies are there for those inclined to genetically edit their plants or pets. Maybe a mouse or *E. coli* genome becomes the next operating system for hobbyists to profitably twiddle. Perhaps this decade will bring a Linus Torvalds or Bill Gates of bio-hackerdom—a hobbyist-turned-entrepreneur who can simultaneously innovate and market his or her DNA-driven ideas.

Management überguru Peter Drucker once remarked that "the purpose of a business is to create a customer." Clearly, the purpose of an innovative business must be to create an innovative customer. To create innovative customers, however, requires companies to inspire more than a few innovative hobbyists. That's what Brooks says iRobot is counting on.



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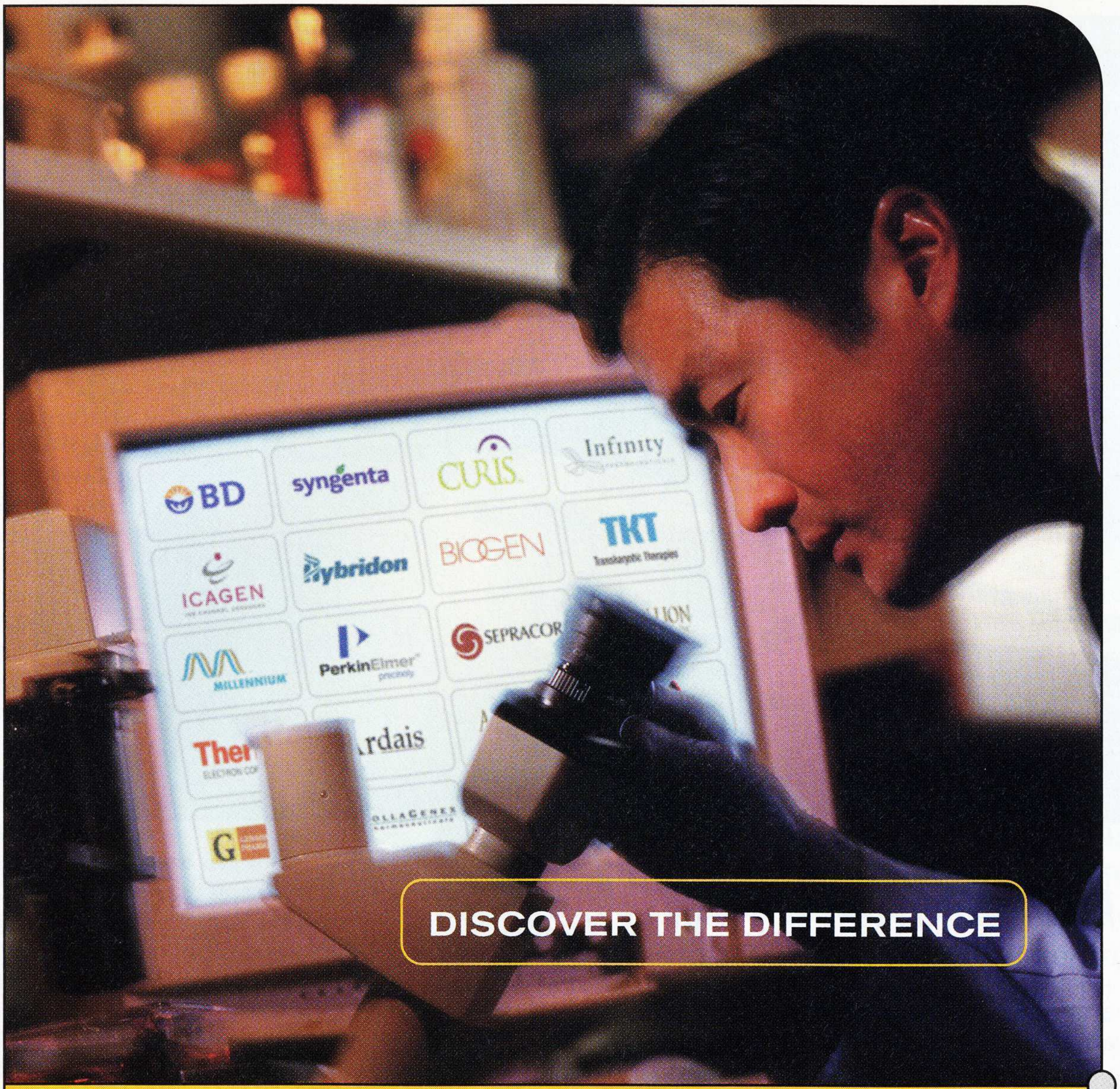
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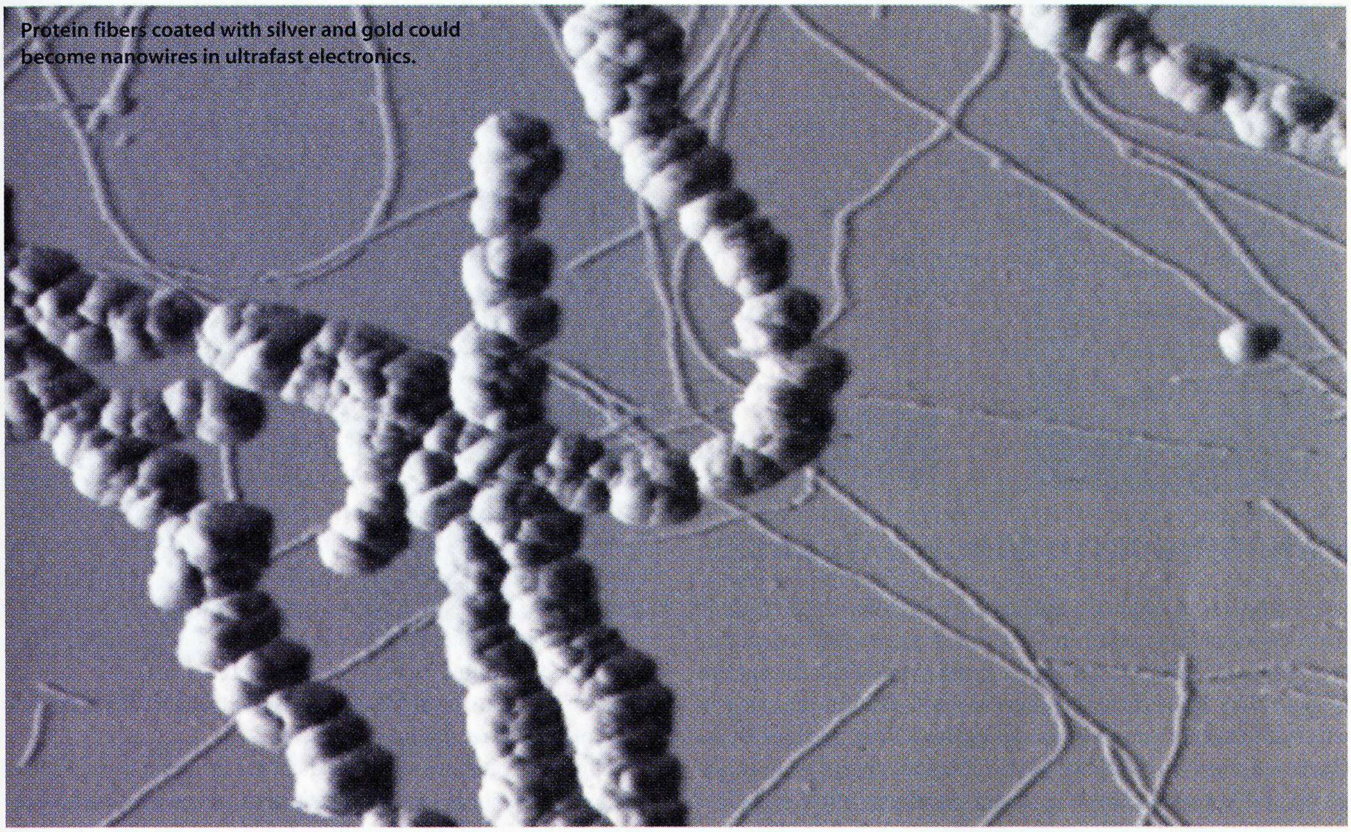

Protein fibers coated with silver and gold could become nanowires in ultrafast electronics.

COURTESY OF THE NATIONAL ACADEMY OF SCIENCES, USA

BIOTECH BOOST FOR NANOELECTRONICS

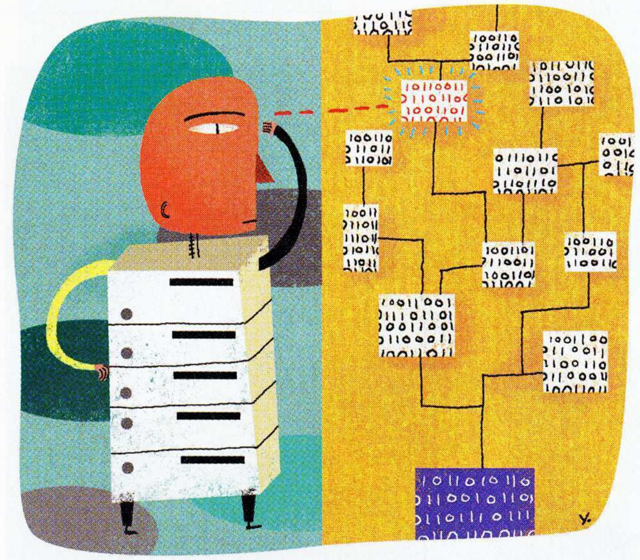
Proteins seen as a versatile platform for making tiny wires

To keep getting faster, electronics must eventually shrink down to the nanoscale. But making wires and switches that small is no easy feat. Biological molecules, with their ability to self-assemble, offer one promising approach. In research done at the University of Chicago, scientists have engineered proteins to form cores for gold wires only 80 nanometers wide.

The researchers started with yeast prions—harmless cousins of the proteins that cause mad-cow disease. Under certain conditions, these prions spontaneously form highly stable fibrils. The team genetically engineered the fibrils to bind tightly to specially prepared gold nanoparticles. The result was fibrils dotted with gold blobs. To fill gaps between the blobs, the team added silver and then more gold, producing conducting wires. "One can imagine using them to build small-scale circuitry for computers, biosensors—there's a whole world of things," says geneticist Susan Lindquist, who collaborated on the project with physicist Heinrich Jaeger in Chicago and is now director of MIT's Whitehead Institute for Biomedical Research. The work was described this spring in the *Proceedings of the National Academy of Sciences.*

The prions have advantages over other biological molecules that researchers have so far tried to use for nanoelectronics. Merging silver with DNA, for example, has allowed scientists to make nanowires, which, thanks to DNA's ability to specifically bind to complementary sequences, can then form circuitlike patterns. But the weak bonds between DNA strands tend to break easily. This is less of a problem for protein fibrils. "We think that proteins offer a whole realm of different capabilities," Lindquist says. Indeed, creating self-assembling nanostructures from proteins "is a very exciting area," says Chris Dobson, a structural biologist at the University of Cambridge in England. His lab is using protein fibrils to build electronic materials and optical materials for telecommunications.

In collaboration with MIT materials chemist Angela Belcher, Lindquist's group is already extending the work. Belcher's lab has developed proteins that can bind to about 30 different electronic, magnetic, and optical materials, and then assemble the materials into structures. The goal is to integrate Belcher's proteins into Lindquist's self-assembly system to create a way to "grow" materials—such as semiconductors—where and in whatever patterns the researchers want. Though it's impossible to predict how long it might take for the new techniques to make their way into industrial use, the research is setting a firm foundation for practical nanotechnology. *—Erika Jonietz*



MANAGING ANTITERROR DATABASES

SOFTWARE | As military and security agencies do everything from coordinating action in Iraq to sifting through telephone and banking records on the home front, they collect mountains of data that are difficult to organize and manipulate, and in which intelligence connections can get lost. Now, database tricks borrowed from the world of particle physics are helping intelligence and law enforcement agencies—and any other organizations that manage large, complex databases—to act on their data more nimbly.

The Stanford Linear Accelerator in Palo Alto, CA, is home to a particle collider that has generated the world's largest database. The company that designed the database, Objectivity of Mountain View, CA, is now attracting a wave of new customers in the areas of defense, telecommunications, and intelligence systems, says Leon Guzenda, the company's chief technology officer. TRW of Redondo Beach, CA (recently acquired by Northrop Grumman), says it uses Objectivity's technology in a data analysis system built for an unnamed U.S. government agency that collects and analyzes scientific data. And SYColeman, a defense contractor in Sherman Oaks, CA, employs the technology in a system for controlling battlefield simulations. While Guzenda says security restrictions prevent him from describing specifics, he says the technology was used to help manage complex military operations in the Iraq war.

These national-security players are all attracted by the same thing: the system's ability to keep complex relationships straight, even as databases swell to mammoth proportions. The underlying architecture of the database—in which data are stored in the form of "objects" that inherit their properties from parent objects in a vast family tree—can bring important connections to light more efficiently than traditional "relational" approaches, where data are stored in the rows and columns of interlinked tables, says Richard Winter, president of Winter Corporation, a database consulting firm in Waltham, MA. The new system has helped scientists keep track of Stanford's particle collision data, which collectively takes up some 700 terabytes (700,000 gigabytes) of storage space, or 35 times as much as the contents of the Library of Congress *(see "Surveillance Nation, Part Two," TR May 2003)*. The "object-oriented" nature of the database makes it easy for scientists to create generations of objects from which more and more of the clutter has been extracted.

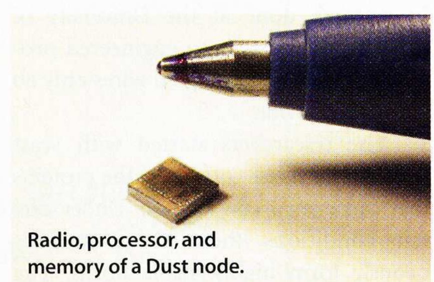
The same qualities make the database tool equally well suited to boosting national security. "Let's say you are monitoring suspected terrorists' telephone calls, e-mails, and the like. The database grows very large, very fast," Winter says. In a relational database, the tables storing this information would form an abstract tangle, but a database like Stanford's would more closely resemble the suspected terrorist network itself. "It can provide a groundbreaking kind of capability," he says. Which means that, as government databases accumulate video surveillance data, communications intercepts, or battlefield intelligence, they'll be able to detect where the data collides. —*Wade Roush*

SMART SPECKS

HARDWARE | **Future wireless networked sensors may, literally, be everywhere, as retail managers put tiny tags on merchandise to track inventory and soldiers sprinkle "smart dust" on battlefields to monitor conditions and threats. Now Dust, a spinoff of the University of California, Berkeley, is close to marketing the world's smallest networked sensors.**

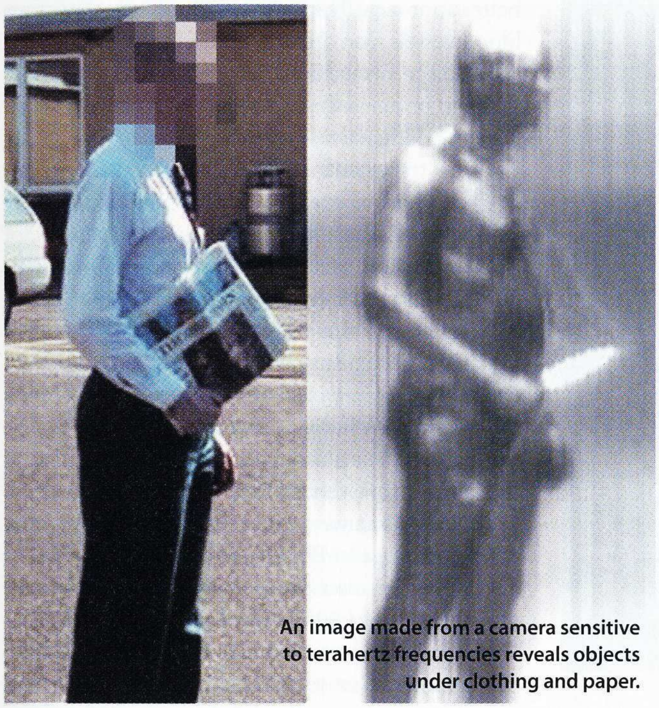
Just four square millimeters, one of the company's "nodes" combines little sensors—which can detect things like temperature, light, or chemicals—with a microprocessor, lithium battery, solar cell, radio transceiver, and memory, all on a silicon chip. It's a "technical tour de force," says Kevin Delin, an expert on sensor systems at NASA's Jet Propulsion Laboratory.

This feat of shrinkage, led by Berkeley electrical engineers Kris Pister and Jason Hill, cofounders of Dust, has as much to do with software as hardware. The software on each node cooperatively manages data storage and transmission with other nodes to minimize overall power consumption. This allows each node to use smaller batteries. The designs of the processor and radio were also optimized to keep power usage to a minimum. Dust plans to commercialize its sensor nodes within a year for customers to test. Other companies, including Intel and Crossbow Technology in San Jose, CA, are also creating tiny sensor nodes. The question now is what applications will take hold. —***Gregory T. Huang***



Radio, processor, and memory of a Dust node.

COURTESY OF JASON HILL AND UC BERKELEY (SPECKS); JAMES YANG (ILLUSTRATION)



An image made from a camera sensitive to terahertz frequencies reveals objects under clothing and paper.

TAMING THE TERAHERTZ

T-rays could be more versatile than x-rays

IMAGING | Just as x-ray technology came along in the 1890s—allowing doctors to peer beneath flesh to see bones and organs—another promising imaging technology is now emerging from an underused chunk of the electromagnetic spectrum: the terahertz frequencies. These so-called t-rays can, like x-rays, see through most materials. But t-rays are believed to be less harmful than x-rays. And different compounds respond to terahertz radiation differently, meaning a terahertz-based imaging system can discern a hidden object's chemical composition. Thanks to this power, "terahertz imaging is getting hotter and hotter," says Xi-Cheng Zhang, a terahertz pioneer at Rensselaer Polytechnic Institute. Potential applications range from detecting tumors to finding plastic explosives. And since t-rays penetrate paper and clothing, a terahertz camera could detect hidden weapons.

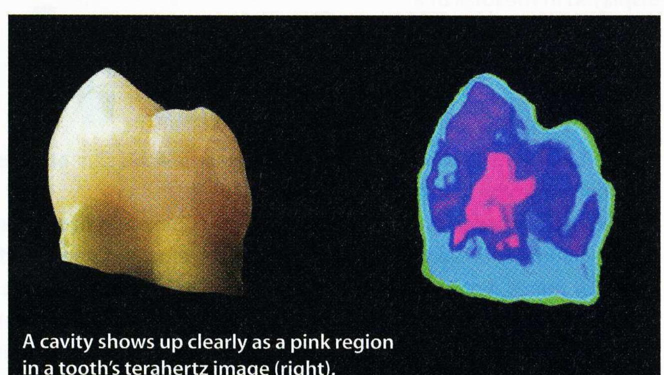
Terahertz frequencies are tough to produce and detect. They're higher than microwaves but lower than infrared light. "You're never sure whether to use electronics-based or optics-based" technology, says Martyn Chamberlain of the University of Leeds in England, a leading terahertz researcher. The terahertz sources now on the market tend to emit many frequencies at once, limiting their utility. In the past year, however, several research projects have made substantial progress in developing devices that produce t-rays within a narrow frequency band—a requirement for precise chemical sensing and medical imaging.

One such system, made by Brattleboro, VT-based Vermont Photonics, works by sending an electron beam across the microscopically rippled surface of a conductor, such as aluminum; the beam causes electrons in the conductor to move up and down the undulations, a motion that shakes loose t-rays. Changing the energy of the electron beam also changes the terahertz frequency generated, says Vermont Photonics cofounder Michael Mross. The company is targeting its instrument primarily at observing interactions involving biomolecules for applications such as drug discovery. Another approach is something called the "quantum cascade laser," a neat bit of semiconductor engineering used to produce infrared light. Moving the technology into the terahertz range requires exquisitely precise control over the materials. Last year, Qin Hu, an MIT electrical engineer, demonstrated a quantum cascade laser that produces a continuous terahertz beam at a well-defined frequency.

The most near-term application for terahertz technology is in medical imaging. In one ambitious effort, TeraView, a Cambridge, England-based startup, has used terahertz imaging to detect skin cancers that elude other imaging technologies—in particular, tumors that form invisibly beneath the surface of the skin. T-rays could also identify unknown biological materials, since biomolecules naturally vibrate at terahertz frequencies, and each has a distinct terahertz "fingerprint." In other words, specific proteins absorb certain characteristic t-ray frequencies, which change their molecular arrangement, or conformation; sensors can then monitor this absorption to indicate the identity of the protein. "Life is a terahertz process," says Chamberlain. One potential application is automated identification of biological warfare agents, such as anthrax. Another is a t-ray chemical sensor, which would take advantage of the fact that other large molecules, such as polymers, also respond to terahertz waves in characteristic ways. A terahertz camera built by QinetiQ of Farnborough, England, takes eerily invasive pictures of people through their clothes.

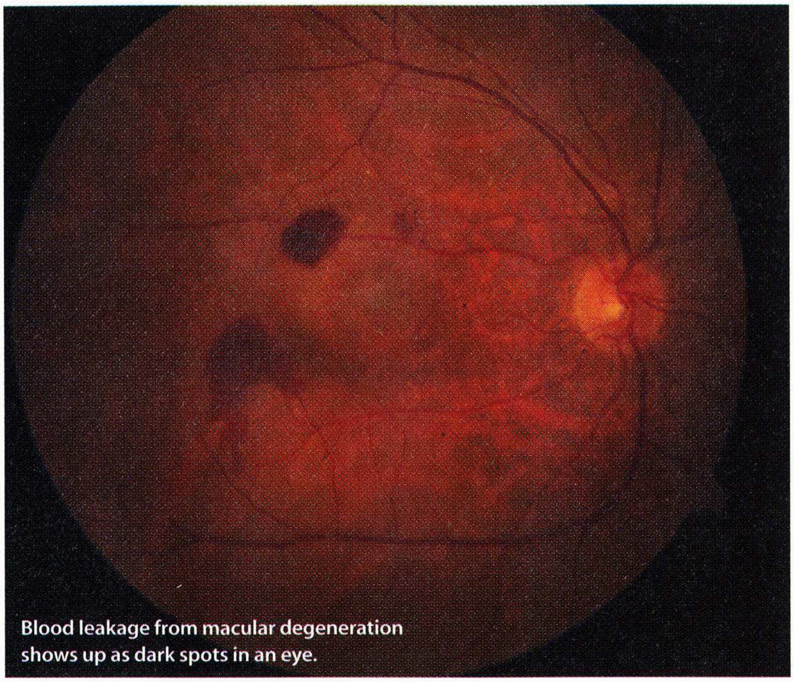
But the interaction of t-rays with proteins raises the question of how safe human exposure is. The European Union is sponsoring a program, called Terahertz Bridge, to study just that. Preliminary results have been encouraging; researchers have seen no evidence of irreversible, x-ray-like tissue damage from the doses of t-rays that would be used for bodily imaging. "So far, it's safe," says Gian Piero Gallerano, coordinator of Terahertz Bridge.

While scientists go through contortions to produce t-rays, nature has it much easier. Terahertz radiation continues to propagate throughout space from its origin in the Big Bang. Says Chamberlain, "The universe is full of this stuff." Before long, humans may begin putting it to practical use. —*Herb Brody*



A cavity shows up clearly as a pink region in a tooth's terahertz image (right).

COURTESY OF TERAVIEW LIMITED, U.K. (TOOTH); COURTESY OF QINETIQ (KNIFE)



Blood leakage from macular degeneration shows up as dark spots in an eye.

NEW VISION FOR EYE DISEASE

RNA-based method thwarts blood vessels

BIOTECH | The leading cause of blindness in the elderly is a progressive eye disease called macular degeneration, which in its most serious, or "wet," form is caused by abnormal blood vessel growth and subsequent blood leakage in the eye. Current treatments use lasers or light-activated drugs to clot these vessels but are generally ineffective; fewer than 3 percent of patients show improved vision following treatment. But in an emerging area of biotechnology, a small New York City company believes it sees a better approach. The key is a biomolecule that stops blood vessels from growing. Injected into the eye, a short piece of artificial RNA, called an aptamer, sticks to proteins that cause abnormal blood vessel growth and inactivates them.

The treatment, which is being developed by Eyetech Pharmaceuticals, showed promise in early clinical trials that ended last year; 80 percent of patients showed stable or improved vision and 26 percent showed significant improvement three months after a single treatment. The drug, called Macugen, "is highly promising," says Nobel laureate David Baltimore, president of Caltech, who counts the treatment among potential new biotech breakthroughs. "It would be a wonderful validation of this unlikely but very powerful technology."

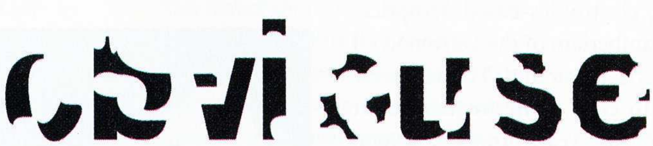
Indeed, aptamers could work against other diseases, too. Regado Biosciences, in Durham, NC, is developing aptamer drugs that treat cardiovascular disease by attacking proteins that cause blood clots. Other companies are in the early stages of searching out aptamers that treat inflammatory disease and infection in a similar, protein-attacking fashion, part of a growing trend toward RNA-based medicine *(see "Prescription RNA,"* TR *December 2002/January 2003)*.

But even if those other applications don't pan out, big bets are being placed on aptamers as a cure for the most serious form of macular degeneration. Last December, Pfizer inked a $745 million licensing deal with Eyetech, which has launched an advanced clinical trial that could eventually lead to approval from the U.S. Food and Drug Administration. To be sure, aptamers are still in their infancy. But it's a technology that may prove visionary. —*Ken Garber*

JAMMING THE SPAMMERS

INTERNET | Junk e-mail operators use programs called bots to register for thousands of free online e-mail accounts. Bot-blocking obstacles offer some protection; Yahoo!'s e-mail sign-up form, for example, asks users to type in an English word that's displayed in the form of a spotty, degraded image that humans can decipher but bots cannot *(see "Excuse Me, Are You Human?" p. 28)*. Trouble is, hackers can build bots that bust such barricades by matching the outline of the word in the degraded image with the outlines of words in a dictionary.

Now there's a new defensive weapon: a tougher visual test. The system constructs English-sounding words, like "brience" and "emperly," then masks them with randomly generated squares, ovals, and polka dots that eat away parts of letters. Human readers can recognize the words. But to break this barrier, hackers would have to crack problems in computer vision and pattern recognition that have remained unsolved for decades, says Henry Baird, the principal scientist at the Palo Alto Research Center in California who developed the system. In tests, the system was impervious to laboratory bots. The new technology bolsters spam-filtering efforts by companies like Microsoft, America Online, and others. Filters can't catch everything, says Brian Cartmell, manager of Spam Arrest, a Seattle company that uses a Web-based visual test like Yahoo!'s to protect customers from junk e-mail. Baird's approach, in contrast, could stop spam artists from creating accounts that send out the junk e-mail. And that could "get us to a point where writing the software to overcome [the test] will be too expensive for it to be worthwhile," Cartmell says. Then we could all stop weeding our in-boxes and go back to being human. —*Wade Roush*



Humans can see this says "obviouse," but computers can't.

COURTESY OF THE PALO ALTO RESEARCH CENTER (SPAMMERS); COURTESY OF THE NATIONAL EYE INSTITUTE, NATIONAL INSTITUTES OF HEALTH (EYE)

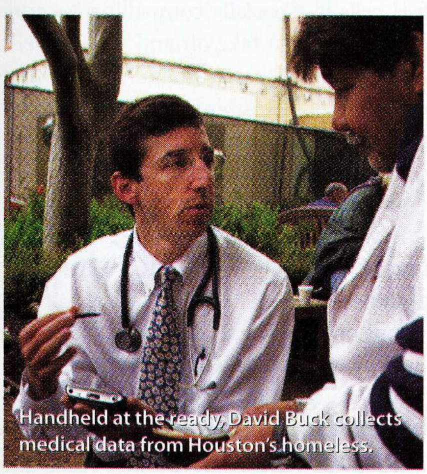
WIRELESS OUTREACH

MEDICINE | While many otherwise sophisticated U.S. hospitals have dithered about adopting them, electronic medical records are enhancing health care for a surprising population: the homeless.

Earlier this year, a nonprofit group called Healthcare for the Homeless-Houston installed five wireless access points around the city that enable fieldworkers, using handheld computers, to view real-time medical records. Rather than lugging paper charts around while doing street outreach, care providers view and update patient records on the spot, using software specially written for personal digital assistants by volunteer David Niemeyer, vice president of technology solutions for Healthlink, a Houston-based health-care consulting firm. The result: easier tracking of difficult-to-find patients and speedier delivery of health care and social services.

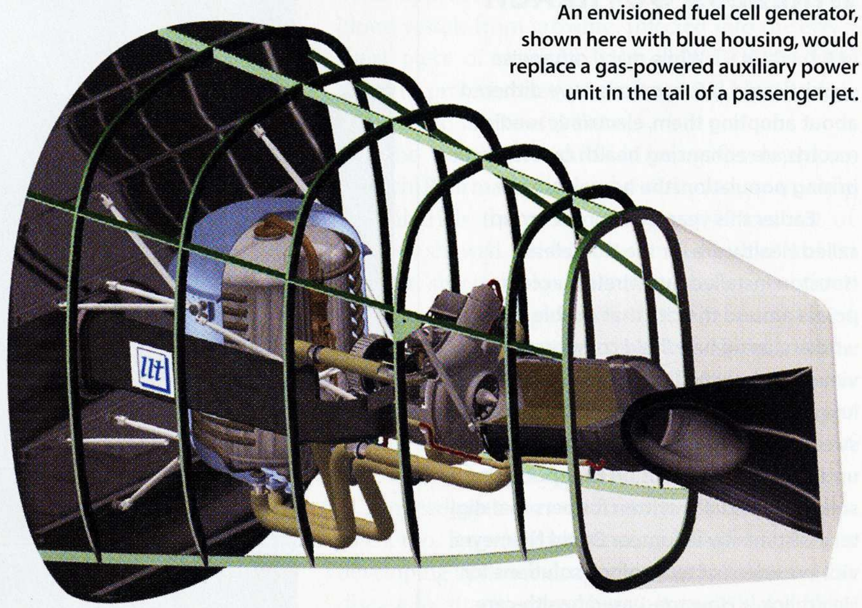
The technology has become "a cornerstone of our work," says David Buck, a family physician at Baylor College of Medicine and president of the organization. What's more, doctors and nurses can tap into indigent patients' medical histories and easily update their records when they show up at a clinic or shelter.

Other cities may soon follow suit. Already, outreach groups in Boston and Indianapolis use electronic medical records. And Buck is making the software freely available to homeless-service agencies in New Orleans and elsewhere. Just don't look for such sophistication at your local hospital, where doctors are probably still scribbling notes on paper pads. —*Erika Jonietz*



Handheld at the ready, David Buck collects medical data from Houston's homeless.

COURTESY OF AGAPITO SANCHEZ/BAYLOR COLLEGE OF MEDICINE (OUTREACH)



An envisioned fuel cell generator, shown here with blue housing, would replace a gas-powered auxiliary power unit in the tail of a passenger jet.

COURTESY OF BOEING

FLYING THE EFFICIENT SKIES

Fuel cells could cut jets' energy consumption, emissions

TRANSPORTATION | Passenger jets on the tarmac are noisy and smelly, kicking out 20 percent of all airport emissions. That's because jets burn fuel in auxiliary power units to generate the electricity that keeps air conditioners and other equipment humming. To take just one example, the auxiliary power unit in a Boeing 777 produces as much smog-causing nitrogen oxide as 155 Chevrolet Impalas.

But a new class of fuel cells, which use solid-oxide technology rather than the proton-exchange-membrane technology favored for cars and small electronics, may eventually do the same job more cleanly—plus allow greater efficiencies in-flight. Solid-oxide cells can use jet fuel as an energy source, and while they're still at the laboratory prototype stage, recent advances have led Chicago-based Boeing and NASA to consider them serious contenders for planes. If all goes well, Boeing will begin developing a tail-mounted fuel cell prototype next year that could be commercialized in about 10 years. "It's going to provide about a two-times improvement in efficiency, and will totally eliminate ground-based emissions coming out of the auxiliary power unit," says Anita Liang, a chemical engineer at NASA's Glenn Research Center in Cleveland, which is helping to develop the devices.

The aircraft application for solid-oxide fuel cells is especially compelling because less fuel lightens the plane, meaning less power is needed to take off and fly. The cells would eventually generate power in-flight, too, replacing the pneumatic systems that suck energy from a jet's engines to power components like cabin-pressurization and anti-icing systems. What's more, aircraft can make use of the fuel cells' chief by-products: water and heat. "There is a potential for getting some synergies out of this," says Dave Daggett, technology leader for energy and emissions at Boeing's facility in Seattle. But despite recent advances, to make it into aircraft, completed fuel cell generators will need to become lighter, cheaper, and more powerful—by about 450 kilowatts, enough to power about 20 houses. But Liang says she expects research being done by NASA—building on work by the U.S. Department of Energy and companies like Delphi, General Electric, and Siemens Westinghouse Power—will deliver the improvements in several years. Volume production and modular designs should make the fuel cells affordable. Much further out, they could power electric jet engines. But for now, it's enough to make airports quieter and cleaner. —*David Talbot*

EXCUSE ME, ARE YOU HUMAN?

If you have signed up for an e-mail account recently, you may have been forced to do something quite demeaning: prove that you are a human being. It's all part of the multipronged war being waged against purveyors of unsolicited e-mail, or spam. But this is one weapon that would best be abandoned.

I saw my first spam back in the 1980s. A typical message was from a California wholesaler offering cheap batteries to everyone in my MIT research group. Many people couldn't understand why I complained. "What's the big deal?" they asked. "Just hit 'delete.'" The big deal, as I saw it, was that unsolicited commercial messages failed a simple test of ethics: if everybody did it, e-mail would become unusable.

Twenty years later, my fears are being realized. Spam has gotten so bad, in fact, that companies are trying to fight it by developing automated approaches for distinguishing humans from computers. They're called "reverse Turing tests," or *captchas*—short for the more descriptive "completely automated public Turing test to tell computers and humans apart." What's driving research on captchas is the realization that a lot of spam is being sent out by automatons: if you can somehow tell the difference between an unattended computer program and one that's driven by a human, you can block the spam while letting through legitimate e-mail.

The irony that we now need to deal with computers masquerading as humans would not be lost on Alan Turing—the computer pioneer who said that a computer could be considered truly intelligent if it could indistinguishably emulate a human being. Rather than evaluating computers to see if they are smart enough, reverse Turing tests are designed to let people prove they are human.

Two popular Web-based e-mail services—Yahoo! and Microsoft's Hotmail—now employ captchas to prevent spammers from automatically signing up for hundreds of mail accounts that can then be used as spam launch pads. A junk-mail blocking service called Spam Arrest uses the technique to filter out machine-generated e-mail. All three services are based on the ability to visually recognize words—something that humans do well and computers do poorly. Sign up for a Yahoo! or Hotmail account, or send e-mail to a Spam Arrest user, and you might be presented with a fuzzy word against a complex and distracting background. To pass this pop quiz, you need to recognize the word and type it into your Web browser.

These tests are the devil. If widely deployed, they will waste our time and confound us—without solving their intended problems. "What's the big deal" this time? After all, Spam Arrest, Yahoo!, and Hotmail each require that you verify your humanity just once, right? After you get your *Homo sapiens* badge, you're free to e-mail all you want. By definition, captchas are *designed* to squander time: sending mail to a Spam Arrest user takes longer than sending mail to someone who doesn't use the service, because Spam Arrest requires that you play its little "prove you're a human" game.

Now imagine sending a message to a mailing list that has a few hundred Spam Arrest users on it. You might need to spend an hour or two completing various tests. By design, there is no way for you to automate your response—that would violate the whole idea. Hotmail might ultimately want to verify that you are a human every morning, to be sure that you haven't turned your account over to a machine.

Moreover, captchas based on visual puzzles discriminate against the millions of people who are blind or who have severe, uncorrectable visual impairment. Yahoo!, aware of this problem, has allowed blind people to register by providing their phone numbers: somebody from Yahoo! verifies their humanity with a phone call. But penalizing the blind with invasive workarounds is hardly an optimal solution.

If captchas really could close the spam spigot, then maybe we could accept them as a necessary evil. They won't. That's

Spam has gotten so bad that companies are trying to fight it with automated approaches for distinguishing humans from computers. These little tests are not only demeaning but ultimately futile.

because captcha creators live in Western countries, where computer power is cheap but human time is expensive, so they're creating tests that can be solved with a small application of human intelligence. But there are many places on the planet where human time is dirt-cheap. Spammers can circumvent the captchas by electronically farming the tests out to China, where a human brain can be hired for about 40 cents an hour. It would be a simple matter to sit a few hundred people down in a room and have them sign up for Hotmail accounts; they could probably register for 20 accounts an hour, or roughly two cents per account. That won't stop the spammers.

Spammers who don't want to hire Chinese labor can set up "free" porno Web sites, where the cost of admission is solving a captcha every few minutes. The spammer then writes a program that goes to Hotmail, signs up for an account, gets a captcha, shows that test to the porn fiend, and supplies said fiend's response to Hotmail. Problem solved!

What's worse, as computers get faster and recognition algorithms get better, captchas will have to get harder to keep pace. Today, you only have to recognize some words on a wavy background. In the future, the task of proving your humanity will likely entail a more convoluted test. If these tests are not nipped now, we are looking at a future where we spend a significant part of each workday proving to machines that we are not machines, too. As a human—and a humanist—I find this possibility deeply offensive. TR

COMPUTERS THAT SPEAK YOUR LANGUAGE

"IWANTTOFLYFROMBOSTONTOMILWAUKEENEXTSATURDAYFORMYSISTERSBIRTHDAYANDIDONTWANT tostopinChicagoandIdontwanttopaymorethanfourhundreddollarsandtheparty startsatthreeoclocksoIneedtogettherebeforethen."

Language-savvy software created by startups Nuance and SpeechWorks automates tasks that once hinged on human conversation. That's generating huge savings in customer service—and inspiring efforts to open the whole digital world to voice interactions, in any language.

Say that to a human airline agent nicely, and he or she will quickly disentangle your words and find flights that meet your criteria. Say it to the airline's automated reservations line, however, and all you're likely to get is a cheery digital voice intoning, "Sorry, I didn't catch that."

Don't blame the voice. Even assuming the airline's computers overcame the garbled words, background noise, and Boston accent to render the request into accurate text, no language-processing system has the computational firepower to make sense of your price and routing constraints, ignore irrelevancies like the fact that Saturday is your sister's birthday, and understand that if the party starts at 3:00 P.M., you're not interested in flights that arrive in Milwaukee at 4:00.

If computers *could* understand and respond to such routine natural-language requests, the results would be win-win: airlines wouldn't need to hire so many agents, and consumers wouldn't have to struggle with the confusion of touch-tone interfaces that leave them furiously tapping the "0" button, vainly trying to reach a live operator.

Futurists have been envisioning such a world since at least 1968, when *2001: A Space Odyssey*'s HAL 9000 became the archetypal voice-interactive computer. Researchers intrigued by the sheer coolness of the idea have been tinkering for just as long with systems for recognizing and responding to human speech. But technologies don't take hold because they're cool: they need a business imperative. For language processing, it's the enormous expense of live customer service that's finally driving the technologies out of the lab. Simple "press or say 'one'" phone trees are rapidly heading for the scrap heap as companies such as Nuance Communications and SpeechWorks, which plans to merge with ScanSoft, meld previously competing strategies into software that infers the intention behind people's naturally spoken or written requests. Major air-

BY WADE ROUSH | ILLUSTRATIONS BY NICK DEWAR


Ability
IODINE
Me
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Negate
2 &
I CANNOT BEAR TO TEAR A BOW
Alpha

lines, banks, and other companies are already using the systems, and while the technology isn't yet as sociable as HAL, it does help callers with simple questions avoid long queues—and frees human agents to deal with more complex requests.

Such improvements have set up natural-language systems for explosive growth: 43 percent of North American companies have either purchased interactive voice response software for their call centers or are conducting pilot studies, according to Forrester Research, a technology analysis firm. As more companies replace their old touch-tone phone menus, today's $500 million market for telephone-based speech applications will grow—reaching $3.5 billion by 2007, according to Steve McClure, a vice president in the software research group at market analysis firm IDC. In late 2002, for example, Bell Canada installed a $4.5 million voice response system built by Menlo Park, CA-based Nuance. "Based on the results we're seeing, the actual return on investment will take only about 10 months," says Belinda Banks, Bell Canada's associate director of customer care. Overall, the company expects to save $5.3 million in customer service costs this year alone.

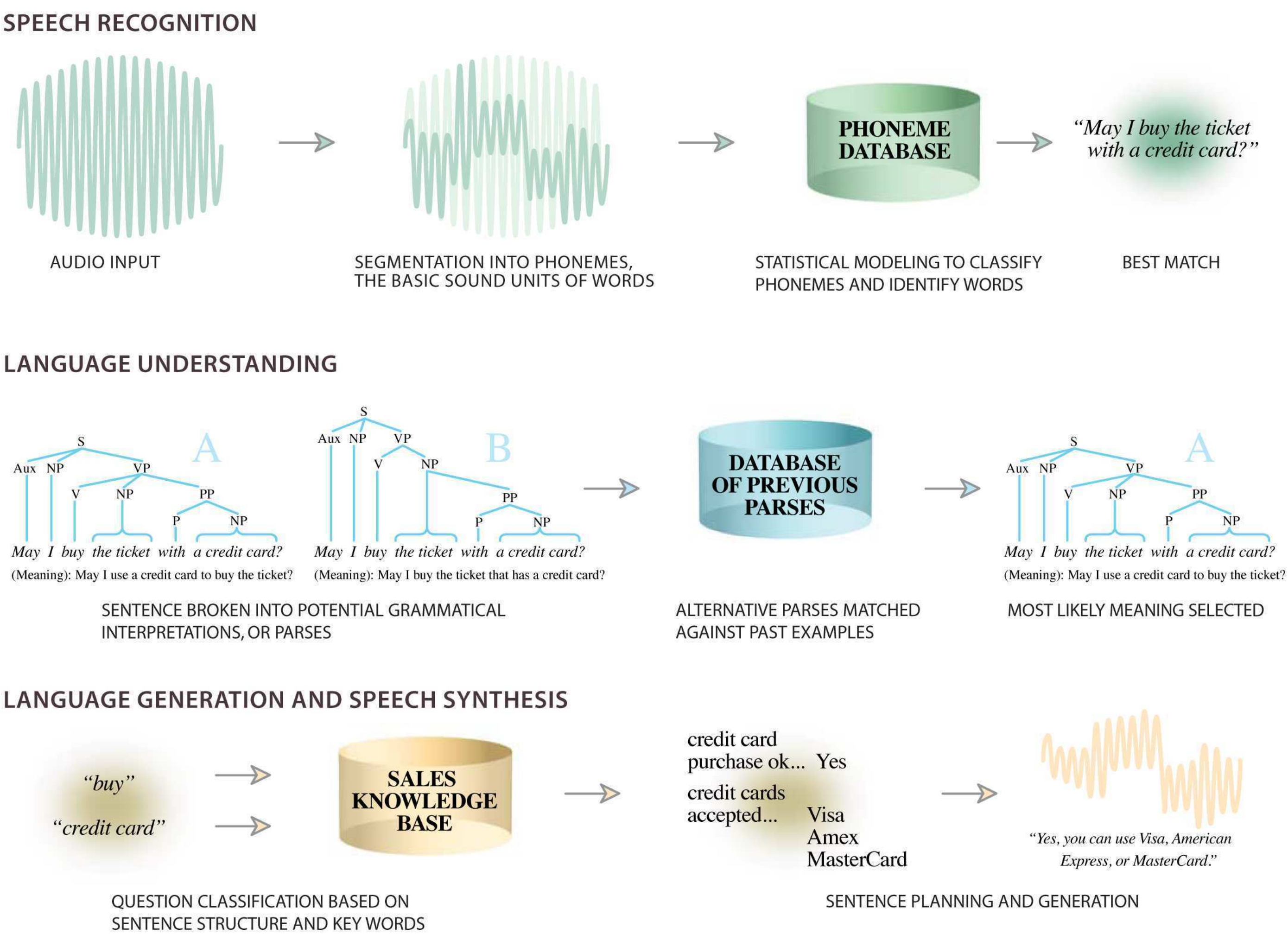
And this is only phase one in the deployment of language-processing systems. Companies like Nuance and Boston's SpeechWorks, the two market leaders in interactive voice response systems, are succeeding partly because they've tailored their technologies for narrow domains—such as travel information—where the vocabularies and concepts they must master are restricted. Even as such systems take over the customer service niche, other companies are still pursuing the challenge of true natural-language understanding. If research efforts at IBM and the Palo Alto Research Center (PARC), for example, bear fruit, computers may soon be able to interpret almost any conversation, or to retrieve almost any information a Web user wants, even if it's locked away in a video file or a foreign language—opening markets wherever people seek knowledge via computer networks. Predicts IDC's McClure, "Whereas the GUI [graphical user interface] was the interface for the 1990s, the NUI, or 'natural' user interface, will be the interface for this decade."

SAY WHAT?

Building a truly interactive customer service system like Nuance's requires solutions to each of the major challenges in natural-language processing: accurately transforming

Inside a Conversational Computer

Each interaction with a hybrid language-processing system involves a series of steps, from understanding speech to generating a response.



SLIM FILMS

human speech into machine-readable text; analyzing the text's vocabulary and structure to extract meaning; generating a sensible response; and replying in a human-sounding voice *(see "Inside a Conversational Computer," p. 34)*.

Scientists at MIT, Carnegie Mellon University, and other universities, as well as researchers at companies like IBM, AT&T, and the Stanford Research Institute (now SRI International), have struggled for decades with the first part of the problem: turning the spoken word into something computers can work with. The first practical products came in the early 1990s in the form of consumer speech recognition programs—such as IBM's Voice Type—that took dictation but forced users to pause after each word, limiting adoption. By the mid-1990s, the technology had advanced and led to dictation systems such as Dragon Systems' NaturallySpeaking and IBM's ViaVoice, which can transcribe unbroken speech with up to 99 percent accuracy.

Around the same time, a few scientists broke away from academic and corporate labs to create startups aimed at tackling the even more complex problems—and bigger potential markets—of the second area of language processing, dubbed "language understanding." It's largely advances in this area that have positioned the field for its real growth spurt. These advances rest on two important realizations, according to SpeechWorks chief technology officer Michael Phillips, a former research scientist at MIT's Laboratory for Computer Science. The first was that there's little point in reaching for the moon—the decades-old dream of systems capable of HAL-like general conversation. "There is a myth that people want to talk to machines the same way they talk to people," Phillips says. "People want an efficient, friendly, helpful machine—not something that's trying to trick them into thinking they're having a conversation with a human." This assumption vastly simplifies the job of building and training a natural-language system.

The second realization was that the time had come to combine philosophies long held by rival factions in the language-processing community. One philosophy essentially says that understanding speech is a matter of discerning its grammatical structure, while the other holds that statistical analysis—matching words or phrases against a historical database of speech examples—is a more efficient tool for guessing a sentence's meaning. Hybrid systems that use both methods, the startups have learned, are more accurate than either approach on its own.

But this insight didn't arrive overnight. At MIT, Phillips had helped develop experimental software that could recognize speech and, based on its understanding of grammar, make sense of a request and reply logically. Like other grammar-based systems, it broke a sentence into its *syntactic* components, such as subject, verb, and object. The system then arranged these components into treelike diagrams that represented a sentence's *semantic* content, or internal logic—who did what to whom, and when. The software was limited to helping users navigate around Cambridge, MA, Phillips explains. "You'd say, 'Where's the nearest restaurant?' and it would say, 'What kind of restaurant do you want?' You would say, 'Chinese,' and it would find you a place."

Shortly after Phillips licensed the technology from MIT in 1994 and left to start SpeechWorks, both he and researchers at competitor Nuance saw that one of their target applications, call steering, required something more. "There are companies out there that have 300 different 800 numbers," Phillips explains.

The Translation Challenge

In the early, post-World War II days of computing, scientists dreamed of creating software so intelligent it could accurately translate one language into another. If computers could crack enemy codes, the thinking went, then why not foreign languages? Five decades later, researchers are still working on the problem. But what was a dream in the 1950s has become an overwhelming demand as business increasingly ignores traditional borders. In fact, by 2007, the already huge translation market—mostly manual today—is expected to reach $13 billion, as advertising, Web pages, and even internal company documents have to be tailored to different countries. "There's so much more text than anybody could hope to translate by hand," says Stephen Richardson, a senior researcher at Microsoft Research, "and it's growing exponentially."

Creating effective translation software requires solving many of the same problems that natural-language processing faces, and then some. Both systems must determine from context whether "light bulb," for example, means a source of light or a less-than-heavy plant bulb. But while customer service software at, say, General Electric could be fairly sure of its interpretation, translation software might have to handle treatises on horticulture as well. Translation software must also contend with idioms whose figurative meaning has nothing to do with their literal meaning—and then find parallel idioms in a different language. It's a problem that makes word-for-word translation impracticable.

Researchers are making progress today using three basic approaches drawn from natural-language processing. Knowledge-based machine translation, for example, relies on human programmers to write lists of rules that describe all possible relationships between verbs, nouns, prepositions, and so on for each language. To generate a sensible translation, the software then scours those rules to find matching words and relationships in the target language. IBM employs knowledge-based software in its WebSphere Translation Server, which the company and its global customers use to rapidly translate e-mail, Web sites, and even real-time chats.

A second approach, example-based systems, relies chiefly on raw computing power. Software algorithms search through millions of words and phrases in documents that already have been accurately translated into multiple languages, compare the translations, and then create an enormous database of vocabulary and word relationships to resolve ambiguity for future translations.

Statistical techniques also depend on computing power to compare reams of previously translated text. However, this strategy selects the most likely translation using sophisticated mathematical models that the software continually upgrades based on how often its interpretations prove accurate. If it correctly translates "light bulb," then the probability score assigned to that phrase for future translations goes up. Microsoft used a combination of example-based and statistical techniques to automatically translate its entire 60-million-word product-support-services knowledge base from English to Spanish.

With accuracy rates hovering between 70 and 80 percent, no system is foolproof. But, says Michael McCord of IBM's Language Analysis and Translation group in Yorktown Heights, NY, translation software significantly reduces the time it takes for humans to translate documents, and sometimes an approximate translation will do. Meanwhile, accuracy rates keep inching up. "More work, bigger machines, more people. We'll get better," he says. *—Chip Walter*

"The customer doesn't understand the structure of the organization—they just know what problem they have. The right thing to do is to ask a question, like, 'What's the problem you're having?'" But compared to a request for a nearby Chinese restaurant, such questions are perilously open ended.

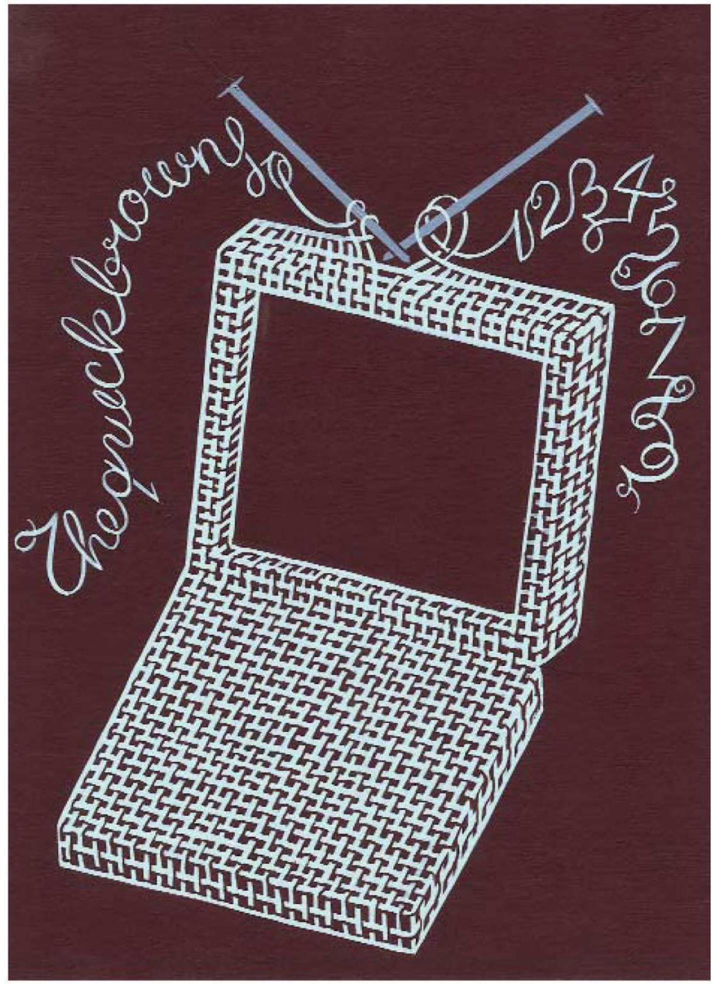
The problem gets harder when one considers that the ambiguity of much human speech—think of a phrase like "he saw the girl with the telescope"—means that many requests are open to multiple interpretations. "There are so many different ways that somebody could speak to the system that trying to cover all that in grammars is prohibitive," says John Shea, vice president for marketing and product management at Nuance.

SpeechWorks finally found a workable solution in 2000, when it married the MIT software with a statistical language-processing technology developed at AT&T Labs-Research in Florham Park, NJ. AT&T's system is built around a database of common sentence fragments drawn from tens of thousands of recorded telephone calls involving both human-to-human and human-to-machine communication. Each fragment in the database is scored for its statistical association with a certain topic and classified accordingly. A fragment such as "calls I didn't make," for instance, might correlate strongly with the topic "unrecognized-number billing inquiries," and the system would route the call to an agent who could credit the caller's account. If the system isn't confident about its choice, it prompts the caller for more information using speech synthesis technology. In the end, according to AT&T, the system correctly routes more than 90 percent of calls—a far higher success rate than callers experience when navigating old-fashioned phone trees on their own.

Nuance developed a similar system, based on technology from SRI, which can use either grammatical or statistical methods, or both, to extract meaning from a caller's speech. "We use different approaches depending on the customer's needs," says Felix Gofman, a product-marketing manager at Nuance. "You can mix and match." In a specific field, such as banking, the topics and vocabulary of callers' questions will be limited, and the system can operate solely using predefined lists of what customers might say. For new or wider-ranging fields such as ordering phone service, the system stores each question it hears in a database, then uses statistical techniques to compare new questions to old entries in a search for probable matches—thereby improving accuracy over time.

SpeechWorks' call center technology is used by such diverse enterprises as Office Depot, the U.S. Postal Service, Thrifty Car Rental, and United Airlines. But the company pushing the technology closest to its limits is Amtrak. Travelers calling Amtrak's automated telephone system can not only get train schedules but also book reservations and charge tickets to their credit cards. "When we set out, the primary goal was to increase customer satisfaction rates," says Matt Hardison, the railroad's chief of sales, distribution, and customer service. But as a bonus, he says, the savings in labor costs repaid Amtrak's $4 million investment in the technology within 18 months.

Nuance, meanwhile, has big customers in the financial and telecommunications industries, including Schwab, Sprint PCS, and Bell Canada. British Airways told the company that after deploying Nuance speech recognition systems last year, its average cost per customer call dropped from $3.00 to $.16. And according to Bell Canada's Banks, 40 percent of customers used

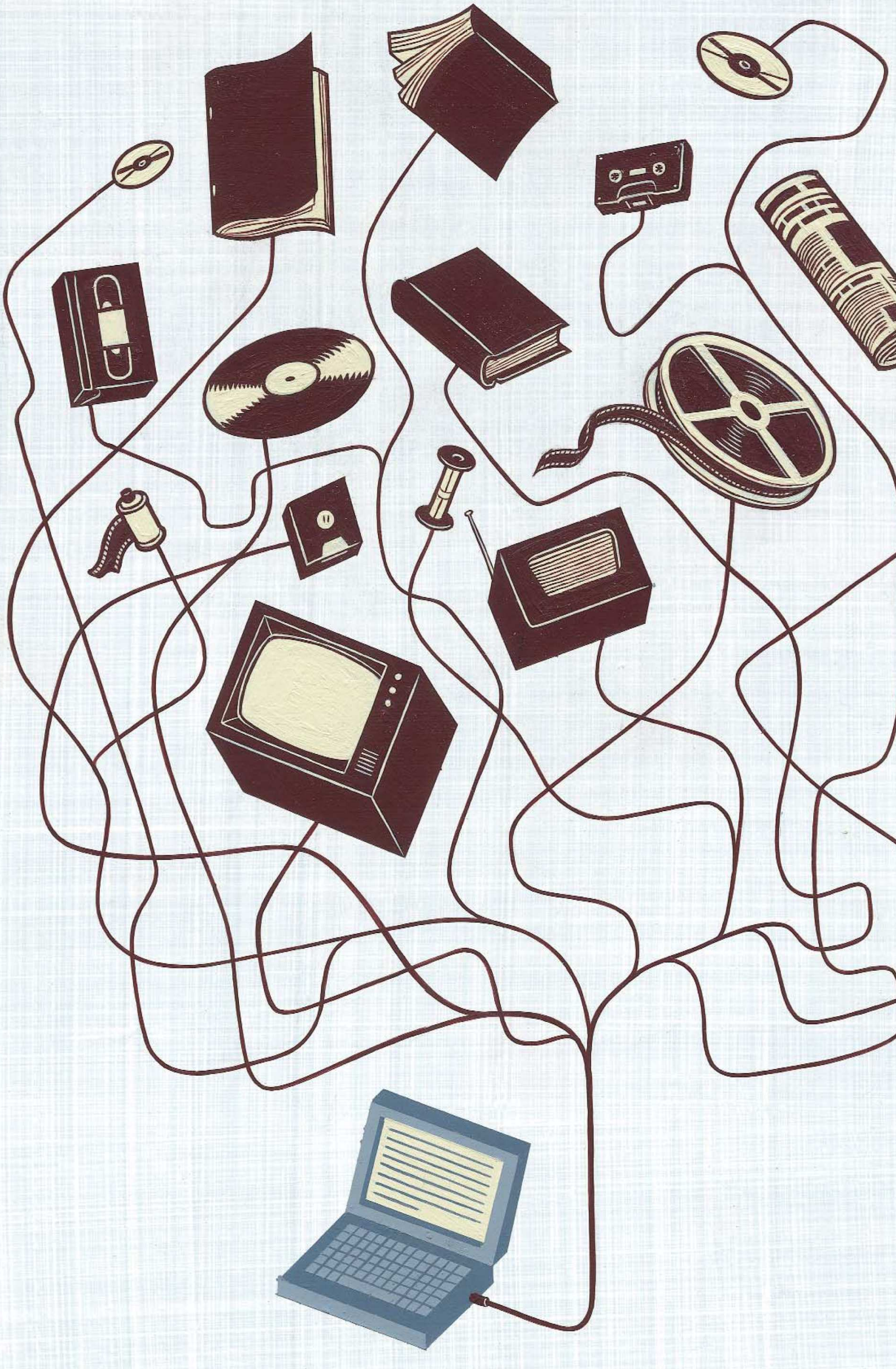


to "zero out," or request a live operator, while navigating the company's touch-tone phone tree. Between the company's December 2002 implementation of the system and March 2003, that number dropped to 15 percent, says Banks.

A DEEPER UNDERSTANDING

For all their success, however, in no sense do these systems really "understand" what they hear. They deal only with rules of grammar, probabilities, and stored examples. Indeed, they excel precisely because their makers have turned away from the quest for a system intelligent enough to read and summarize a book or sustain a general conversation.

But other researchers retain a broader view of the possibilities for natural-language processing. Like Ron Kaplan, a research fellow at PARC who developed much of the basic grammatical theory behind many of today's natural-language systems, they are building software that can cope with a far greater variety of inputs—from newspaper stories to the disorganized mass of multimedia information on the Web. Kaplan is critical of what he calls the "shallow methods" used for niche applications like call steering. "Compared to the alternative"—maintaining a costly staff of human customer-service agents—"they are actually not bad," he says. "But compared to what you would like, they stink." A more effective natural-language interface, Kaplan says, would eliminate the need to carefully tailor the systems and allow users to speak or write freely.



Two problems hindering that vision, in Kaplan's view, are that the databases of language samples upon which simpler systems draw are too small, and the statistical algorithms they use are designed to eliminate the ambiguity in much of what people say, homing in as quickly as possible on the most likely meaning. Kaplan believes that if this ambiguity is eliminated too soon, the correct meaning of an utterance—especially a long or complex sentence—may be lost. So he has spent the last decade working on a grammar-driven system, called the Xerox Linguistic Environment, which actually tries to *preserve* ambiguity. The system parses an utterance into every possible sentence diagram allowed under a set of 314 rules governing relationships between various parts of speech (PARC researchers assembled the rules manually over three years). A complex sentence with 40 or more words, for instance, might be interpreted in as many as 1,000 different ways.

The system's grammar analysis is so thorough that it correctly captures, on average, 75 percent of the logical relationships in a sentence—which is "actually very high compared to what most statistical methods do," says Kaplan. That accuracy rate can be increased to about 80 percent if the software takes advantage of those statistical methods, comparing each possible interpretation to similar diagrams in a "trained" database—in the PARC software's case, a store of hundreds of thousands of accurate diagrams of sentences drawn from *Wall Street Journal* articles.

Kaplan plans to first unleash the system on Xerox's huge digital knowledge base of copier repair techniques, which is constantly consulted and updated by the company's field technicians. There it will compare thousands of individual entries in order to weed out redundancies and contradictions. "It could be that a lot of technicians have discovered the same solution to a common problem," such as replacing a copier's drum, Kaplan explains. "You get a bunch of entries saying the same thing, only in different ways." Finding and pruning out such redundancy automatically, he adds, can help technicians spend less time sorting through options. The software could also eventually become the core of an advanced system for translating documents into different languages—a task particularly plagued by ambiguity *(see "The Translation Challenge," p. 35)*.

Before a computer can understand or translate stored information expressed in natural language, however, it has to find it. That's getting more difficult as the digital universe expands—which is why IBM is pursuing an ambitious project to employ natural-language processing in the management of "unstructured information," the mass of digital text, images, video, and audio stored on computer networks. Much of IBM's business rests on its database product, DB2, but a traditional database can only retrieve information that has already been organized and indexed. IBM wants to give business users and consumers immediate access to the unindexed data languishing on millions of hard drives around the world, effectively extending its dominance in structured-data management into the realm of unstructured information. To get there, the company is pursuing an initiative designed to merge different language-processing approaches into powerful software that can intelligently search, organize, and translate all this data. The project, called the Unstructured Information Management Architecture, could fuel the company's business well into the Internet age. "As research bets go, this is a big one," says Alfred Spector, the division's senior vice president.

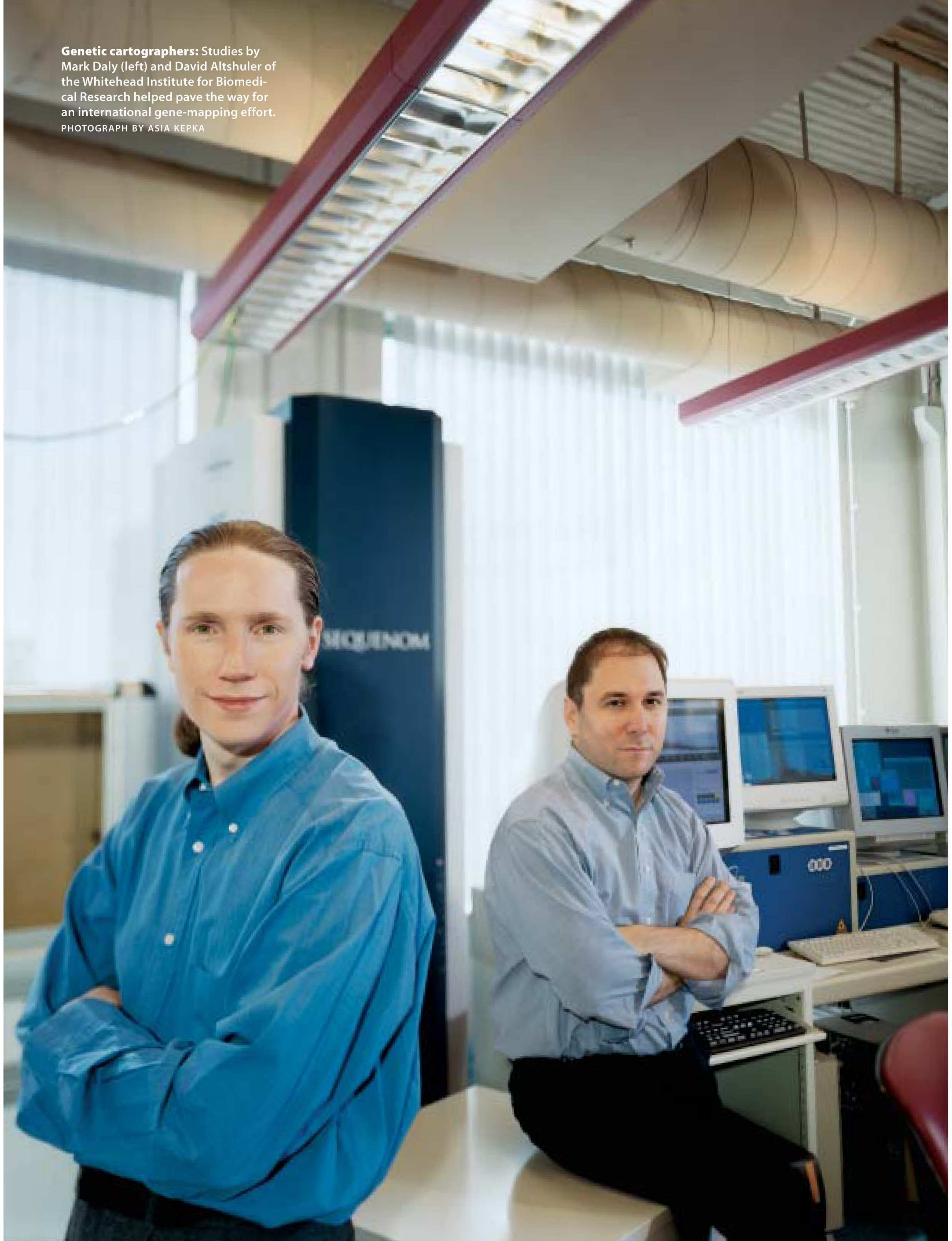
Translation software and other products that use the new architecture are still in the prototype stage. But ultimately, says David Ferrucci, the project's lead software architect, the architecture will help IBM build systems that pluck the latest information a user wants from any digital source, in any language, and deliver it in organized form. Already, U.S. companies spend $900 million a year on "enterprise information portals" that help employees find the records they need, according to Giga Information Group in Cambridge, MA, and the opportunities for IBM and other companies developing software for managing unstructured information will only multiply as that information accumulates. "There is now clearly a business rationale to deal with unstructured data," concludes Spector.

If efforts to cope with ambiguity, unstructured information, and other complexities of language succeed, we might ultimately stop treating computers like toddlers, simplifying everything we say to fit their immature understanding of the world. When that day comes, and it could come soon, consumers can expect to find automated voice interfaces at every turn, allowing them to use plain English (or French or Chinese) to interact with everything from Web archives to appliances and automobiles.

And that would really be something to talk about. TR

Language Processing's Babel

COMPANY	TECHNOLOGY	LOCATION
AT&T	Automated speech recognition; natural-sounding speech synthesis	New York, NY
Banter	Automated e-mail classification and response	San Francisco, CA, and Jerusalem, Israel
IBM	Automated speech recognition; translation; standard architectures for managing unstructured information	Armonk, NY
Intel	Audiovisual speech recognition	Santa Clara, CA
Inxight	Software for discovering, exploring, and categorizing text data on corporate networks	Sunnyvale, CA
iPhrase Technologies	Natural-language text searching of corporate Web sites	Cambridge, MA
Microsoft	Grammar checking; query interfaces; translation	Redmond, WA
Nuance Communications	Interactive voice response systems for telephone-based customer service	Menlo Park, CA
Palo Alto Research Center	Improved algorithms for extracting meaning from written text	Palo Alto, CA
SpeechWorks (merging with ScanSoft)	Interactive voice response systems for telephone-based customer service	Boston, MA
StreamSage	Natural-language search and indexing of video and audio material	Washington, DC



Genetic cartographers: Studies by Mark Daly (left) and David Altshuler of the Whitehead Institute for Biomedical Research helped pave the way for an international gene-mapping effort.
PHOTOGRAPH BY ASIA KEPKA

BY DAVID ROTMAN

GENES, MEDICINE, AND THE NEW RACE DEBATE

ADVANCED GENOMIC TOOLS ARE NOW CATALOGUING THE GENETIC DIFFERENCES BETWEEN PEOPLE AROUND THE WORLD. THIS GENETIC MAP COULD PROVIDE DOCTORS AND DRUGMAKERS WITH NOVEL WAYS TO TREAT COMMON DISEASES LIKE DIABETES AND SCHIZOPHRENIA. IT IS ALSO RAISING PROFOUND QUESTIONS ABOUT ETHNICITY AND RACE.

Poring over the raw genetic data, Mark Daly noticed a startling pattern. An expert in statistical genetics and a fellow at MIT's Whitehead Institute for Biomedical Research, Daly was scouring a region of human chromosome 5, a place that colleagues strongly suspected contained a gene that puts people at risk for a devastating digestive condition called Crohn's disease.

The sequence spelled out in the DNA letters A, T, G, and C was almost identical in all the samples Daly examined—each from a different person. As Daly expected, sprinkled every thousand letters or so were spots where a single letter tended to vary from one person to another. Then came the surprise. Many of these single-letter variations seemed to occur together, as if they were tightly linked across long stretches of the DNA. In other words, whenever Daly looked at an individual copy of one of the sections of DNA and found an A at one of these positions, he would find a G at the

next one, about a thousand letters away, a C in a third position still further down the line, and so on. After roughly tens of thousands of letters, another pattern began; the long stretches of linked variants, it seemed, divided the chromosome into neatly defined blocks. What's more, for any given stretch of the chromosome, there were only four or five versions of these blocks that kept showing up in the different individuals Daly studied. Daly realized he was staring at evidence of an underlying structure to the human genome. He was also looking at the beginnings of biology's next big project—and its next big controversy.

identifying all 10 million of a person's specific single-letter variants—a time-consuming and prohibitively expensive task—researchers could simply pinpoint a telltale letter for each block and then know the other variants around it.

But first they would need a map, one that identifies the boundaries of blocks and the different versions of each block found in populations around the world. Last October, a year after Daly's discovery, the world's top genetic researchers—including scientists from the Whitehead, the National Institutes of Health, Johns Hopkins University in Baltimore, the University of Tokyo, the Beijing Genomics Institute, and Cambridge, England's Wellcome Trust Sanger Institute—formed a $100 million, three-year plan to chart just such a map. It's called the International HapMap Project, and beginning with several hundred blood samples collected from Nigeria, Japan, China, and the United States, it will use highly automated genomics tools to parse out the common haplotype patterns among a number of the world's population groups *(see "Shining Light on Variations," p. 44)*.

"This is really a natural outcome of having the sequence of the human genome," says Aravinda Chakravarti, director of the Institute of Genetic Medicine at Johns Hopkins and a leading participant in the international consortium. "Now we want to know what part of the genome varies. Knowing the variations that enhance or retard specific diseases will be a tremendous value" for medicine, he says. "Having a catalogue of the variations will be very helpful. And the more global the catalogue is, the more helpful it will be."

The hope is that as disease researchers and epidemiologists compare the genetics of patients with ailments such as asthma or schizophrenia to those of healthy people, the map will guide them to the differences in genes or combinations of genes that put a person at risk. Not only can such information be critical in forewarning at-risk individuals, it can also provide invaluable clues to drug developers searching for the biological mechanisms that cause the diseases.

The most immediate impact of the HapMap, though, is likely to be the prediction of how a patient will respond to a drug *(see "Startups Seek Genomics' Killer App," p. 48)*. Adverse drug reactions cause more than 100,000 deaths each year in the United States alone. And, says David Goldstein, a geneticist at the University College of London, identifying the genetic factors underlying different responses to drugs could lead to quick and easy tests to screen patients. "There is absolutely no doubt that the haplotype map will help," he says. "Even if that's all the HapMap does, it will be a critical contribution to medicine."

CRITICS WORRY THAT THE DATA WILL BE MANIPULATED TO GIVE CREDENCE TO ETHNIC STEREOTYPES, TO REVIVE DISCREDITED RACIAL CLASSIFICATIONS, AND TO FUEL BOGUS CLAIMS OF FUNDAMENTAL DIFFERENCES BETWEEN GROUPS.

At about the same time, in the fall of 2001, several other genetic researchers reported similar findings. Much of the human genome, it soon appeared, consists of what researchers began to refer to as haplotype blocks. And as Daly had seen on chromosome 5, the blocks tend to come in a limited number of common varieties, which suggests that the genetic variants that put people at risk for common diseases might also be widely shared. Overall, the findings suggested a far simpler structure for the human genome than had previously been supposed. "It is a fundamental change in how we view genetic variations," says Daly. "And for once, the genetics are very favorable toward performing disease studies."

Indeed, the finding has immense implications for understanding and treating diseases such as diabetes, schizophrenia, and hypertension. Though people share roughly 99.9 percent of their genes, it is precisely that other one-tenth of a percent that plays a role in determining why one person gets schizophrenia or diabetes while another doesn't, why one person responds well to a drug while another can't tolerate it. If, in fact, the variable DNA letters occur in a limited number of easy-to-identify, blocklike patterns, it would give geneticists a practical way to quickly and cheaply search for the complex genetic variations related to common diseases and different drug responses. Instead of

Despite its promise, though, the HapMap carries with it some potential dangers, particularly at a time when race is again becoming a hotly debated issue in the practice of medicine. Physicians routinely make clinical decisions assuming genetic differences based on individuals' perceived race. And what some call the "first ethnic drug," a heart disease treatment specifically meant for African Americans, is headed to market; several other drugs are also targeting specific racial groups. How the genetic insights gleaned from the HapMap are wielded in this growing controversy will be critical.

The use—and often misuse—of genetics to explain racial and ethnic differences is, of course, nothing new. But the HapMap, together with a series of powerful genomic tools developed over the last several years, will make it possible to spell out in great detail the genetic differences between peoples from different parts of the world. Sociologists, bioethicists, and anthropologists worry that the genetic data could be manipulated to give an air of biological credence to ethnic stereotypes, to revive discredited racial classifications, and even to fuel bogus claims of fundamental genetic differences between groups.

"Here's the rub," says Troy Duster, a sociologist at New York University. The

The negotiator: Howard University epidemiologist Charles Rotimi is working with Nigerian community leaders to obtain genetic samples from one of Africa's oldest ethnic groups.
PHOTOGRAPH BY ERIKA LARSEN

haplotype project "wants to make sure it has a range of population groups" so that its results are widely applicable. The danger, he says, is that some people will inevitably extend any genetic differences found in specific populations to broad racial groups. Others share Duster's concerns. Geneticists will find differences between geographically distinct groups, says Jonathan Kahn, a bioethicist at the University of Minnesota. And when such differences come to light, he suggests, "It's all too easy for biological and genetic categories to become conflated with racial ones. And when they do, a lot of mischief can occur."

Avoiding the genetic analysis of different populations is not the answer either, says Duster. "If you don't sample sub-Saharan Africa, people will say, 'Wait a minute, you've got to go to Africa.'" How to map differences between various populations while avoiding the dangers of racial stereotypes, says Duster, "is a conundrum without an answer."

COMMON COMPLAINTS

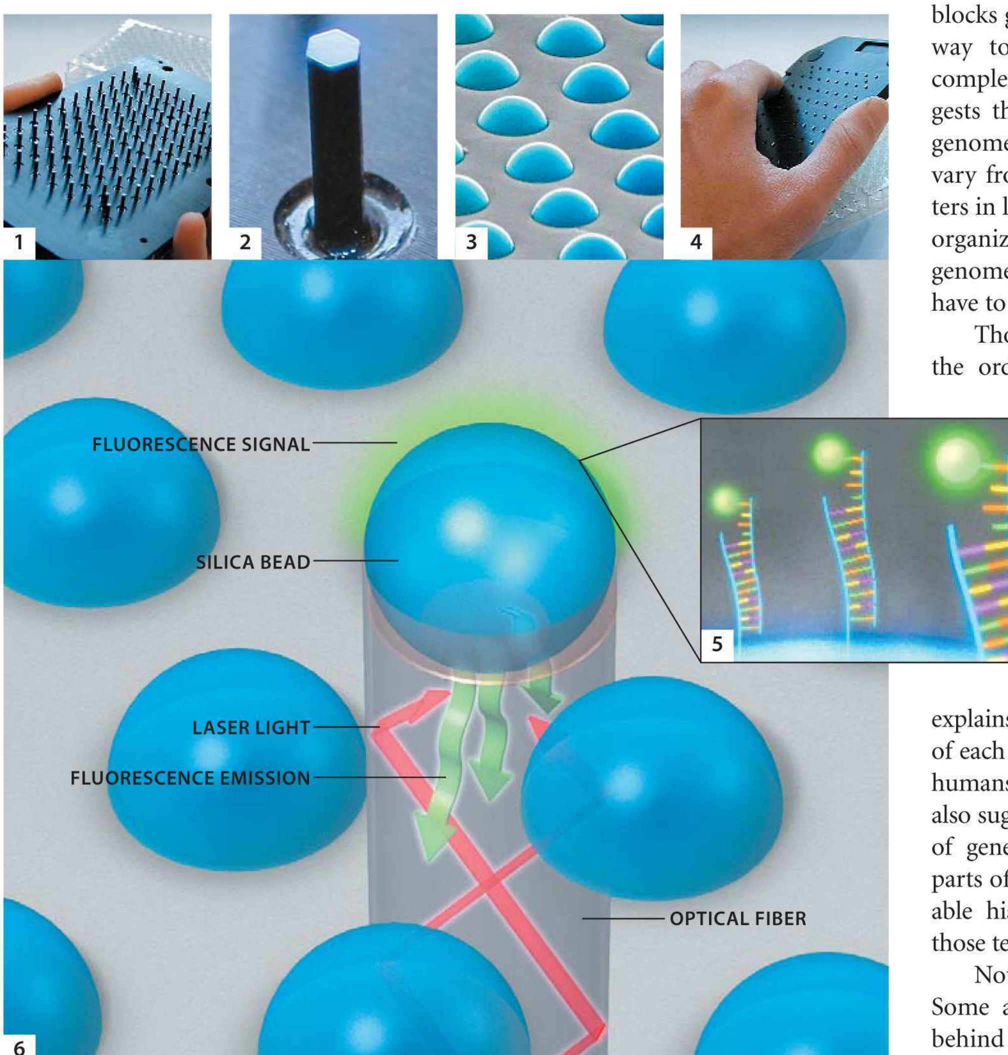
The HapMap provokes such excitement in the medical community largely because the hunt for disease-causing genes has hit a stone wall. Despite successes in finding the genetic culprits for some rare and deadly disorders, such as cystic fibrosis and Huntington's disease, which are caused by lone genes, researchers have had a difficult time finding the genes behind common diseases, like schizophrenia, diabetes, hypertension, and alcoholism. Geneticists suspect that some combination of dozens or even hundreds of genes contributes to each of these disorders. Tracking down a single rogue gene is already like hunting for a needle in a haystack. But understanding how patterns of variations among individuals and populations correlate with common diseases is "fantastically more complex," says College of London's Goldstein.

The discovery of the haplotype blocks gives medical researchers a useful way to navigate this mind-boggling complexity. The evidence, says Daly, suggests that, in fact, most of the human genome consists of these blocks, which vary from 10,000 to around 50,000 letters in length. It is a structure that neatly organizes the three billion letters in the genome and one that "doesn't necessarily have to be the way it is," says Daly.

Those pushing the HapMap believe the orderly, blocklike structure of the genome is more a reflection of history than of any biological function. They suspect that most variations in single DNA letters date back many tens of thousands of years and have been inherited intact generation after generation, along with neighboring stretches of DNA. This explains why only a few common versions of each block are likely to be found, since humans share a limited set of ancestors. It also suggests that comparing the patterns of genetic variation found in different parts of the world can provide a remarkable history of human migration over those tens of thousand of years.

Not all geneticists, however, buy it. Some argue that much of the science behind the haplotype project remains speculative. Numerous questions still swirl around the blocklike structure, maintains Kenneth Kidd, a geneticist at Yale University School of Medicine in New Haven, CT. Doubts remain about how to define the boundaries and, even, how widespread the blocks are through-

Shining Light on Variations



San Diego, CA's Illumina has developed one of the automated technologies used by the HapMap project to spot specific genetic variants. 1. Illumina's technology uses an array of 96 bundles of optical fibers. 2-3. A bundle comprises 50,000 fibers, each capped by a three-micrometer-wide silica bead coated with DNA probes. 4. The array is dipped in a standard 96-well microplate containing the test samples of fluorescently tagged DNA. 5. Different DNA sequences bind to the probes on each particular bead. 6. Using a laser and an optical sensor to read the fluorescence, the assay determines the presence of a targeted sequence.

ILLUSTRATION: JOHN MACNEILL; SOURCE AND PHOTOGRAPHS: ILLUMINA

THERE'S NOT ENOUGH ART IN OUR SCHOOLS.

NO WONDER PEOPLE SAY "GESUNDHEIT" WHEN YOU SAY

"TCHAIKOVSKY."

If one were to make a quick list of the world's favorite composers, despite his relatively recent vintage Peter Ilyich Tchaikovsky would be on it. After all, he did compose *Swan Lake*, which is perhaps the most famous ballet of all time. And there can't be more than just a handful of ballet companies that don't perform *The Nutcracker* every Christmas.

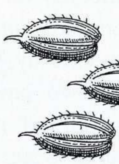


Fig. 1 Pollen

Causes watery eyes. Much like Tchaikovsky's composition "Romeo and Juliet."

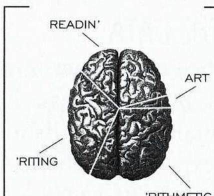
Peter Ilyich Tchaikovsky endured many setbacks, not the least of which was a blind barber.

Indeed, this great Romantic composer should be so immortalized. As a young man, he pursued a career in music at enormous personal risk and against his own father's advice. His mild temperament combined with his tendency to work too hard left him with insomnia, debilitating headaches and hallucinations. On top of that, Tchaikovsky's composition teacher never liked his work, even after he became world-famous.

Setbacks like these could have finished a lesser man. Instead, they informed his work, which remains some of the best loved in history. Yet some kids will still confuse Tchaikovsky with a nasal spasm.

Why? Because the arts are slowly but surely being eliminated from today's schools, even though a majority of the parents believe music and drama and dance and art make their children better students and better people.

To help reverse this disturbing trend, or for more information about all the many benefits of arts education, visit us at AmericansForTheArts.org. Or else Tchaikovsky could seem like just another casualty of allergy season.



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DORIS DUKE CHARITABLE FOUNDATION

out the genome, says Kidd. What's more, he contends, the HapMap's premise that there are consistent patterns of genetic variation around the world is likely wrong and that there will be "tremendous" differences. "There are likely to be few universal blocks," he says. The haplotype map, he adds, "is being touted as great for all populations, but I don't think it will be."

There are also doubts about whether the HapMap is even looking for the right genetic culprits. William Thilly, an MIT geneticist, says that for numerous conditions known to be caused by mutations in a single gene, there are dozens to hundreds of different mutations in that gene that have been found to cause the same disease. Thilly argues that genetic risks for common diseases are caused by a "spectrum" of relatively rare mutations scattered over unknown genes throughout the genome. He points out that many common diseases afflict diverse populations that display markedly different haplotypes. In other words, the HapMap's effort to detail common patterns in genetic differences and link those differences to diseases is largely a wild-goose chase.

FOLLOWING THE DATA

In his small office in a corner of a busy research lab at Boston's Massachusetts General Hospital, David Altshuler, a physician and expert on diabetes, is full of restless energy. Six floors below, gridlock has brought the traffic coming in and out of the sprawling hospital to a maddening halt. But Altshuler, who is also the director of medical and population genetics at the Whitehead Institute and a prime mover behind the HapMap project, can barely sit still. The critics of the HapMap in the genetics community clearly have him peeved.

"They're nihilists. All they say is, 'Don't do it.' I don't believe it's a panacea, but it's a useful tool," says Altshuler. He points to the failure of many critics to propose a feasible alternative as particularly frustrating. "Ultimately, all of genetics boils down to measuring the genetic variation in some population of people and comparing it to their characteristics and looking for correlations. That's all genetics ever is." And, adds Altshuler, the HapMap "is simply a tool to study genetic variation at unprecedented levels of accuracy and detail."

Altshuler freely acknowledges that many scientific questions remain about how genes vary among individuals and populations and even about how effective looking at patterns of common genetic variations will be in tracking down risk factors for diseases. But, he adds, the HapMap offers a direct route to testing ideas about the genetics of common diseases. "For that reason alone," he says, "it is an important investment."

One issue to be resolved is how extensively human populations share specific versions of haplotype blocks. Geneticists do know that some differences between populations are a consequence of their migrational history. They expect, for example, that the length of haplotype blocks in populations from Africa will be shorter than those in populations of European or Asian origin. That's because humans originated in Africa and migrated throughout the rest of the world, starting around 50,000 years ago. Thus, the genetic history of populations in Africa is older and, since their genes have had a far longer time to vary, the linked blocks have had more of a chance to break up into smaller segments. It is also likely that any migration out of Africa did not include representatives from all groups, so geneticists expect to find more diversity in Africa.

Altshuler and his colleagues found strong evidence that this is precisely the case in a preliminary study they did of the haplotype patterns of nearly 300 people, including African Americans, people from Nigeria, and volunteers with European, Japanese, and Chinese ancestry. In a paper published last summer in the journal *Science*, the researchers described finding most of the common haplotype varieties in all the populations, though samples from Africa showed the greatest diversity and also tended to have shorter haplotype segments. The paper's conclusion: while there are some differences, the boundaries of the haplotype blocks and the common versions are largely shared across populations.

"I DON'T BELIEVE IT'S A PANACEA," THE WHITEHEAD'S DAVID ALTSHULER SAYS OF THE HAPMAP. IN HIS ESTIMATION, THE MAP "IS SIMPLY A TOOL TO STUDY GENETIC VARIATIONS AT UNPRECEDENTED LEVELS OF ACCURACY AND DETAIL."

A STARTING POINT

These days, Charles Rotimi is frequently en route from his office in Washington, DC, to Nigeria to carry out delicate negotiations with community leaders and residents that will permit the HapMap project to begin gathering blood samples. The Yoruba people of western Nigeria are one of Africa's largest and oldest ethnic groups, and a perfect starting point for the HapMap project.

Rotimi, a genetic epidemiologist at Howard University's National Human Genome Center, is hoping the HapMap can provide genetic details that will greatly facilitate his research on how people with shared ancestry vary in their reactions to drugs and susceptibility to common diseases. Specifically, Rotimi is interested in pinning down why populations of the African diaspora in various parts of the world suffer from dramatically different rates of diseases like hypertension, diabetes, and obesity.

For example, in results gleaned from conventional epidemiological studies during the last few years, Rotimi has found that about 7 percent of blacks living in rural Africa and 14 percent of those living in urban Africa suffer from hypertension, while 34 percent of African Americans have the condition. "We see drastically different rates of disease in those that share common ancestry," says Rotimi. "We're seeing very clearly that the current environment is the most important factor." But he believes the HapMap could shed new light on this result. "We've made assumptions about the underlying genetics" of the different populations, says Rotimi. It might turn out, he says, that the HapMap reveals previously unrecognized "subtle differences in genetic patterns" that could help him

better interpret the disease findings. For example, he says, if the patterns of the haplotype blocks in the populations are sufficiently different, it could be a key clue to understanding genetic factors underlying disease risks.

It is just these types of studies that point to the ethical complexities raised by the HapMap and other new genomic methods. On one hand, looking for genetic variations among racial groups runs the danger of reinforcing old stereotypes. Yet genetic differences and similarities in populations with shared ancestry are frequently observed and can provide a powerful tool for understanding diseases; they may even help researchers pinpoint nongenetic factors, like diet and the environment, that influence who contracts a disease. At least according to some, the use of broad racial categories in genetic studies may actually help turn up social, environmental, and cultural reasons for health disparities among different groups.

Last summer, Neil Risch, a leading population geneticist at Stanford University, gained national attention by publishing a paper in an online journal called *Genome Biology* calling for the use of five racial categories in genetic studies. The paper attacked a growing consensus among researchers that racial classifications are neither genetically valid nor useful. Risch's contrarian conclusion: differences in drug responses and disease risks need to be separately examined in each of the five racial groups. Otherwise, he warned, genetic research will tend to ignore issues peculiar to minority groups.

No sooner had Risch's paper begun stirring up the race debate in the genetics community than a group of researchers headed by Marcus Feldman, a prominent population biologist at Stanford, published an article in *Science* that reported detailed data on gene samples from individuals from 52 populations. The research group sorted the samples using both an advanced genomic ap-

Startups Seek Genomics' Killer App

While the detailed genetic information produced by the International HapMap Project will very likely be a boon for medicine, a few ambitious biotech startups have no intention of waiting around for the map to be completed. Late last year, Perlegen Sciences, a Mountain View, CA-based company, completed its own version of a haplotype map and is already using it to tackle one of the pharmaceutical industry's most intractable problems: why people respond so differently to the same drug.

The reasons a drug might cure one patient while failing to help, or even poisoning, another are varied and complex. But using its preliminary haplotype map, and working with several large pharmaceutical partners, Perlegen is conducting a series of tests to compare the genomes of individuals to their drug reactions. The goal, says chief scientist David Cox, "is a bar code" of sorts. The information will spell out the specific genetic variations that are correlated with a safe and beneficial response to the drug, as well as those variants associated with a negative response. From that, says Cox, it should be straightforward to design a simple screen to test patients before they are given a particular treatment.

Such a screening test could be the genomics industry's killer app. Numerous drugs are kept off the market because they produce dangerous side effects in a small, though significant, percentage of people; others are only effective in a limited population. A reliable test to identify how a patient will respond could open new markets for numerous drugs, says Cox, who left his position as codirector of the Stanford University Genome Center to help found Perlegen in 2001. "If you can get a drug on the market, it's worth a billion dollars."

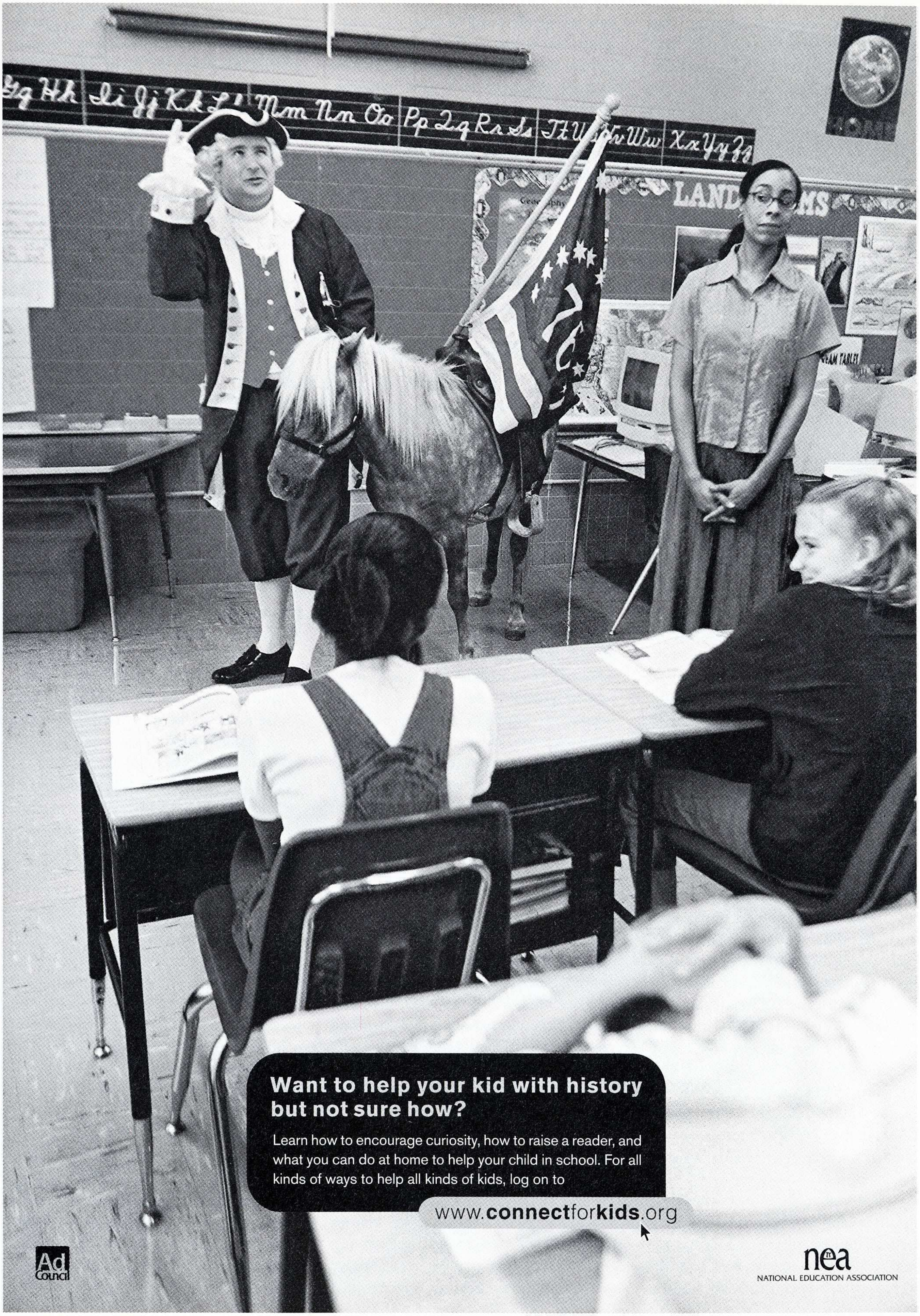
That's a number that gets the attention of investors and drugmakers, even in today's skeptical business climate. And it has made Perlegen one of genomics' hottest startups. Earlier this year, despite a disastrous venture capital market, the company raised $30 million in private investments, which came after a 2001 round of venture financing that totaled $100 million. Since last fall, Perlegen has entered into a series of collaborations with large drugmakers, including GlaxoSmithKline and Bristol-Myers Squibb.

Perlegen is not alone in pursuing the vision of connecting genetics with drug responses *(see "The Tool Makers," below)*. While the startups vary in approaches and business strategies, they share an ambition: using highly automated genomic tools to cheaply rifle through an individual's DNA to find genetic variants that will be useful in tailoring better treatments. New Haven, CT's Genaissance Pharmaceuticals, for example, has just completed a study of hundreds of people to pinpoint genetic markers that predict how individuals vary in their response to different cholesterol-lowering drugs.

Call it cautious bravado, but Perlegen's Cox is convinced that, at least at his company, the strategy of scanning for genetic variations is about to make a real contribution to medicine. "We're not popping any champagne corks till we've changed lives," he says. But, he's quick to add, those corks could begin flying within the next few months.

The Tool Makers

INSTITUTION	TECHNOLOGY	STRATEGY
Illumina (San Diego, CA)	Fiber-optics-based tools to scan for genetic variations	Sell instruments to large drug companies and genomics labs
Genaissance Pharmaceuticals (New Haven, CT)	Mapping haplotypes and genes associated with certain diseases	Market database of haplotypes and genes to large pharmaceutical makers
Perlegen Sciences (Mountain View, CA)	Microarrays to scan for genetic variations	Collaborate with drug companies to examine variations associated with diseases and drug responses
Sequenom (San Diego, CA)	Mass spectroscopy to rapidly scan for genetic variations	Sell instruments to large genomics labs; identify disease genes
ParAllele Bioscience (South San Francisco, CA)	A "single-tube" assay to scan for genetic variations	Develop technologies for genomic researchers to use to scan genomes for variations


Want to help your kid with history but not sure how?
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proach and self-reported ancestry. They found that the genetic samples fell generally into five geographic categories: Europe, Africa, East Asia, Oceania, and the Americas. They also found that how people categorized themselves—whether they called themselves black or white or Asian—correlated closely with the genetic categories.

Yale's Kidd, one of the coauthors of the *Science* paper, notes that following its publication, some observers argued that the findings demonstrated the existence of races as biological entities, while others maintained that the data proved the opposite. "My opinion is closer to the latter," says Kidd. The results, he explains, show that it is possible to detect very small genetic differences between different populations if you look closely enough. "There is a bit of history that is recoverable," says Kidd. "But that doesn't support the idea of race. It does support that when you look around there is some geographical structure that is present in the genome, though it's extremely small."

While the interpretation of the results might be in doubt, the paper, and today's advancing genetic tools, clearly mark the reentry of mainstream genetics into the debate over race and how to best categorize populations.

DOES RACE MATTER?

The U.S. Food and Drug Administration is now deciding whether to approve a controversial heart disease treatment called BiDil that is specifically meant for African Americans. (The drugmaker, NitroMed of Bedford, MA, claims that blacks are twice as likely as whites to suffer heart attacks.) This new "ethnic drug" is far from an anomaly. Earlier this year, the FDA proposed guidelines prescribing that all drugs in development be evaluated for varying effects on different racial groups.

As genomic tools improve, and there is an increasing emphasis on pharmacogenetics (the use of information about genetic variations to predict a drug's safety or effectiveness), the debate over race and genetics will be most vigorously played out in the medical arena. Race, of course, already plays a huge role in how doctors diagnose and treat patients. Physicians are well acquainted with the idea that Caucasians with northern-European ancestry have higher rates of cystic fibrosis than Asians and blacks, while African Americans suffer from higher rates of hypertension and diabetes.

"Race is used all the time. It's part of a doctor's calculations," says Mildred Cho, codirector of Stanford's Center for Biomedical Ethics. But the downside to using race as a way to view genetic differences, she says, is that it tends to oversimplify a person's complex genetic makeup. "It may seem like a good shortcut, but it can be misleading. It's a shortcut to nowhere." Most differences will be relative, she says. Imagine, for example, that researchers find that 60 percent of Asians fail to metabolize an enzyme, while 40 percent of Caucasians fail to do so. In terms of treating a particular patient, she points out, the results "are clinically not very helpful." Similarly, she argues, new drugs like BiDil are "jumping the gun" by targeting specific races "without the necessary understanding of underlying biological causes" of disease differences.

The hope is that the HapMap and other new, advanced genomic methods will help clarify complex genetic differences and, eventually, give physicians the tools to profile the genetics of each person and use that information to guide treatment decisions. If you want to know how to medically treat a person, you need information about him or her, says London's Goldstein. "Only in the ignorance of that," he says, "do you think about the population and flop on a racial label and say, 'That's good enough.'"

It is into these turbulent waters that the HapMap is diving. And while on one level it is only a tool to help determine specific DNA variants, the project will almost inevitably play a critical role in future debates over race, medicine, and genetics. Whether it plays a productive role—helping to destroy stereotypical concepts of race—or whether it is manipulated by those wishing to gain genetic credence for racist agendas, is still anyone's guess.

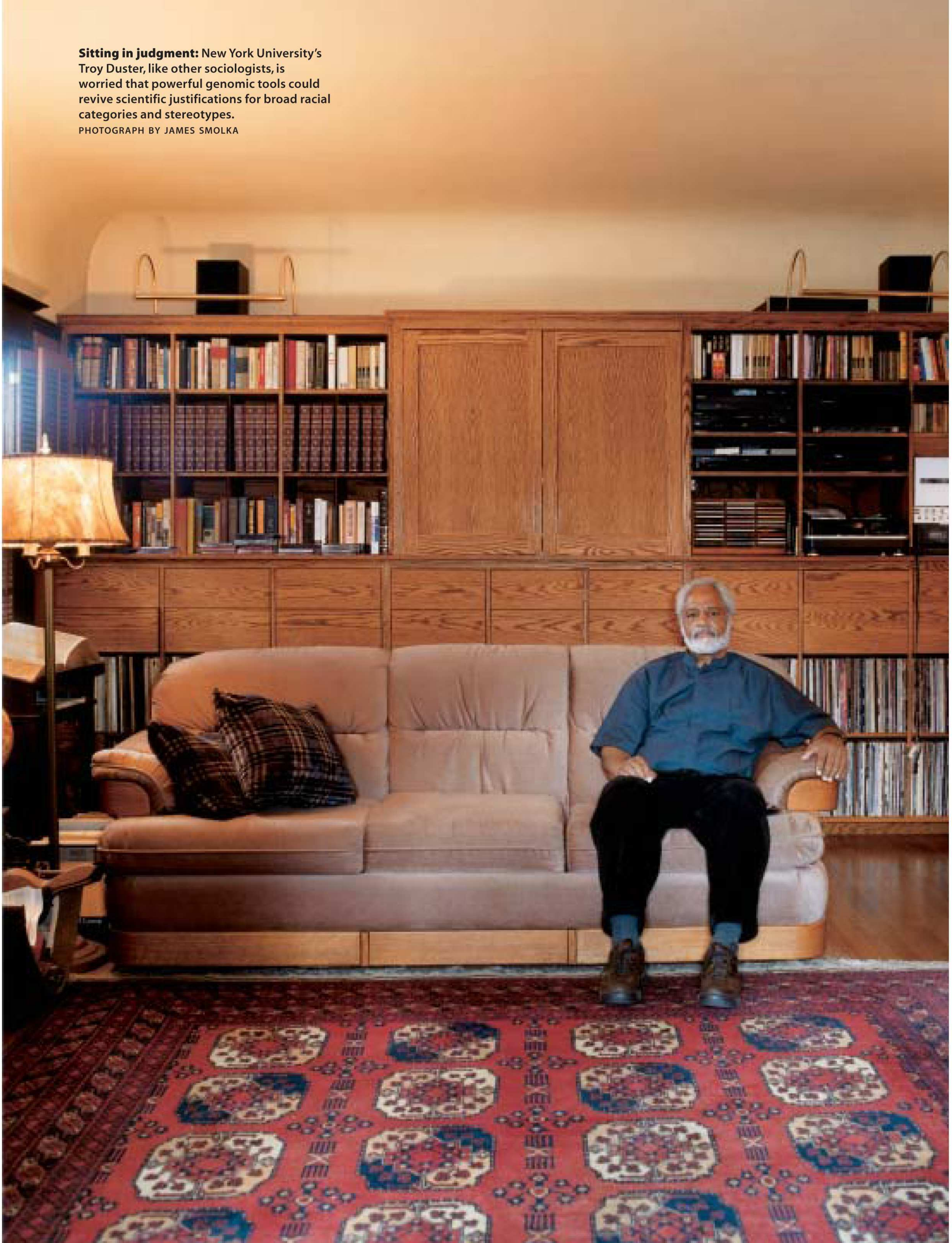
What does seem certain is that the HapMap will produce surprises and scientific insights into human variation that both scientists and the public will struggle to understand. And like any cartographers exploring unknown geography, HapMap researchers will surely happen upon some tricky terrain. The discovery several years ago, for example, that a series of mutations in the cancer genes BRAC1 and BRAC2 were particularly common in Ashkenazi Jews raised widespread fears about how these findings could be used to stigmatize Jewish people. Imagine the potential for social harm if the HapMap produced genetic data that eventually revealed that a specific population has a propensity, say, for alcoholism or schizophrenia.

"I'm not a naysayer" to the HapMap project, says NYU's Duster. "But I feel it is fraught with all kinds of dangers." Those involved, he says, need to be particularly sensitive to how the genetic variations are explained to the public. "There *will* be differences" between populations, he says. "The wrong way to proceed is to report the differences as more profound than they are and with consequences for anything other than the particular disease."

Participants in the project say that they are aware of these dangers, but that the potential benefits justify the risks. Altshuler points to the years he has spent treating diabetes patients and facing the frustration of not being able to offer a solution. "The reason that I do this research is that the most striking thing about medicine is how little we know, how little we have to offer patients for common diseases."

If the HapMap fulfills its potential to help medical researchers and physicians better navigate the treatment of common and devastating diseases, like diabetes, schizophrenia, and hypertension, it will have been dangerous ground well worth exploring. TR

AS GENOMIC TOOLS IMPROVE, THE DEBATE OVER RACE AND GENETICS WILL BE MOST VIGOROUSLY PLAYED OUT IN THE MEDICAL ARENA. THE HOPE IS THAT GENOMIC ADVANCES WILL UNRAVEL THE COMPLEX CAUSES OF DISEASE.



Sitting in judgment: New York University's Troy Duster, like other sociologists, is worried that powerful genomic tools could revive scientific justifications for broad racial categories and stereotypes.
PHOTOGRAPH BY JAMES SMOLKA

Singing in the rain: Meteorologist Paul Douglas founded Minneapolis-based Digital Cyclone to provide people with custom weather forecasts, which they can receive on Web-enabled mobile phones.
PHOTOGRAPH BY CRAIG PERMAN

Pinpoint Weather

CHEAP COMPUTER POWER, NEW MATHEMATICAL MODELS, AND THE LATEST OBSERVATION SYSTEMS ARE PRODUCING ACCURATE, HIGH-RESOLUTION FORECASTS. WEATHER-SENSITIVE COMPANIES ARE BENEFITING, AND YOU CAN GET THE DATA PERSONALIZED ON YOUR HANDHELD DEVICE. BY DAVID H. FREEDMAN

TELEVISION METEOROLOGIST Paul Douglas remembers the day back in 1997 when he had the inspiration that led to the launch of his company. He had predicted on-air a rainstorm moving through Minnesota's Twin Cities, only to be confronted off-air by a flood of e-mails from local viewers wanting to know how the storm might affect their plans for the day. "It was so frustrating," he recalls. "'What time will it start raining in my town?' 'I'm driving north; will I beat the rain?' 'My wedding is this afternoon; will it be rained out?'"

Douglas was helpless to answer such queries. His forecast was based largely on information from the National Weather Service, which predicts the conditions for a 12-kilometer by 12-kilometer area and whose predictions have nothing to say about how the weather varies within that area. And even if Douglas could make such localized forecasts, there was no way he could disseminate the personalized information effectively. And then it hit him: maybe he could give everyone a customized weather report. Two years later, in 1999, he founded Minneapolis-based Digital Cyclone, which predicts weather events over six-kilometer-by-six-kilometer areas and offers the information over mobile phones.

Digital Cyclone is just one of several companies taking weather forecasting to new levels of usefulness and precision. The Weather Channel in Atlanta, GA, for one, now provides eight-kilometer-resolution maps and an alert service for desktop computers. And AccuWeather in State College, PA, generates one-kilometer-resolution weather maps that are available on personal digital assistants and Internet-enabled phones. Fed by the availability of vast reservoirs of cheap computer power, new mathematical techniques for fine-tuning weather models, and high-tech observation systems, these firms are exploiting the much neglected facet of weather forecasting Douglas calls the "short game": that is, advising people about the particular weather conditions in their individual neighborhoods or towns, not just their regions.

COURTESY OF METEORLOGIX

The move to such higher-resolution forecasts could translate into huge savings. According to John Dutton, dean emeritus of Pennsylvania State University's College of Earth and Mineral Sciences, over $3 trillion of the nation's annual economy is affected by weather events. Farmers, construction workers, snow removal crews, energy maintenance workers, railroad dispatchers, and truck drivers depend on accurate and precise forecasts to effectively manage their time and resources. An unexpected cool air mass on a summer day could stick a power company with millions of dollars of unused electricity. A change in wind speed could modify a farmer's choice to spray fertilizers, which can disperse and even ruin neighboring crops in winds above 11 kilometers per hour. A minor temperature difference can determine whether a snow removal crew will lay down sand or salt. Salt is generally only effective above -7 °C, and a wrong decision to use it can not only be ineffective at reducing ice but also waste thousands of dollars of taxpayers' money.

"Whether it's for employees or soccer moms, there's an insatiable demand for weather information," says Douglas. "A lot of incredibly useful information is already available, but there's a real opportunity to filter it, make it more timely and detailed and accurate, and provide it in more useful form."

Personalized Forecasts

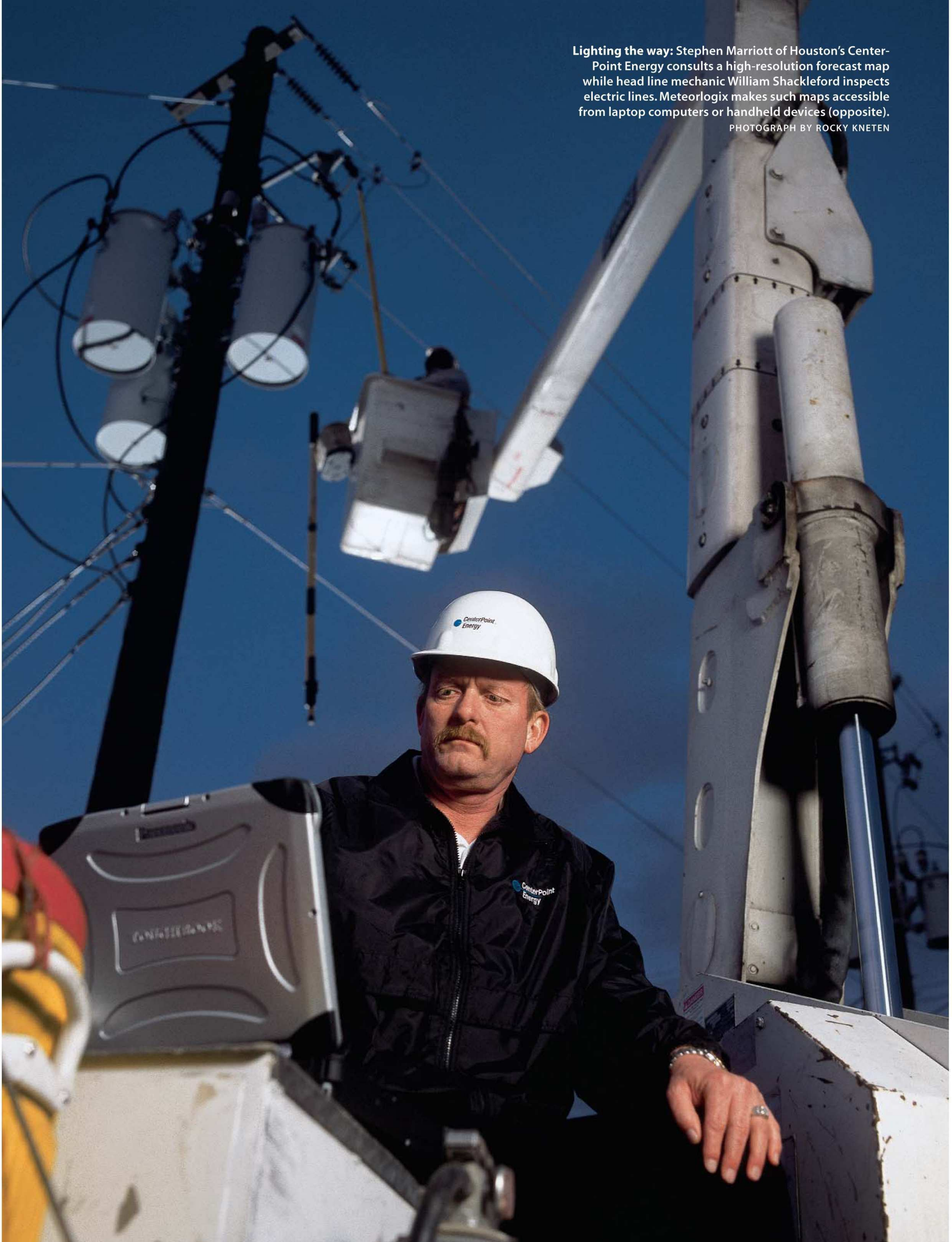
For five decades, weather forecasting in the United States has relied on models that run on the latest computer technology at the National Weather Service's National Center for Environmental Prediction in Camp Springs, MD. The models use more than 100 million daily measurements of temperature, moisture, air pressure, wind speed, and wind direction gathered from different locations around the world. Based on this data, forecasts are calculated on global, national, and regional scales every six hours for areas as small as 12 kilometers by 12 kilometers.

Real weather, of course, can vary quite a bit over distances as short as a few kilometers, says Craig Burfeind, a meteorologist who cofounded Digital Cyclone with Douglas. "Winter storms can have a precise line, and a few miles to either side of that line can mean the difference between rain and six inches of snow." Burfeind notes that one day this past winter, temperatures in the southern suburbs of Minneapolis hit the low 20s C (70s F) while the northern suburbs remained around freezing—resulting in temperature differences of 6 °C or more over a six-kilometer range. And Minneapolis isn't even near a large geological feature, such as a mountain or a valley, that can affect wind speed and direction, humidity, and temperature, and create measurable differences across a small area. Even a sizeable body of water can create sharp temperature contrasts that contribute to lake-effect snow, heavy coastal fog, or unexpected thunderstorms.

The Weather Service would be happy to produce forecasts for everyone's locale if it were practical. But increasing the resolution of the forecast grid to, say, six kilometers by six kilometers actually requires eight times as much calculation. "Our next step in that realm is to 10 kilometers, which won't be operational until the end of 2004," says Lauren Morone, operations officer at the National Center for Environmental Prediction.

But there is another way. In the 1990s, researchers at Pennsylvania State University began incorporating the raw data collected from the National Weather Service into their own PC-based models. "Running a model used to be a large centralized operation, like the Manhattan Project," says Penn State climatologist Paul Knight. In contrast, he says, the new generation of PC models complete fewer calculations for a smaller area of the globe and are therefore able to produce high-resolution, localized weather forecasts that can be churned out relatively quickly.

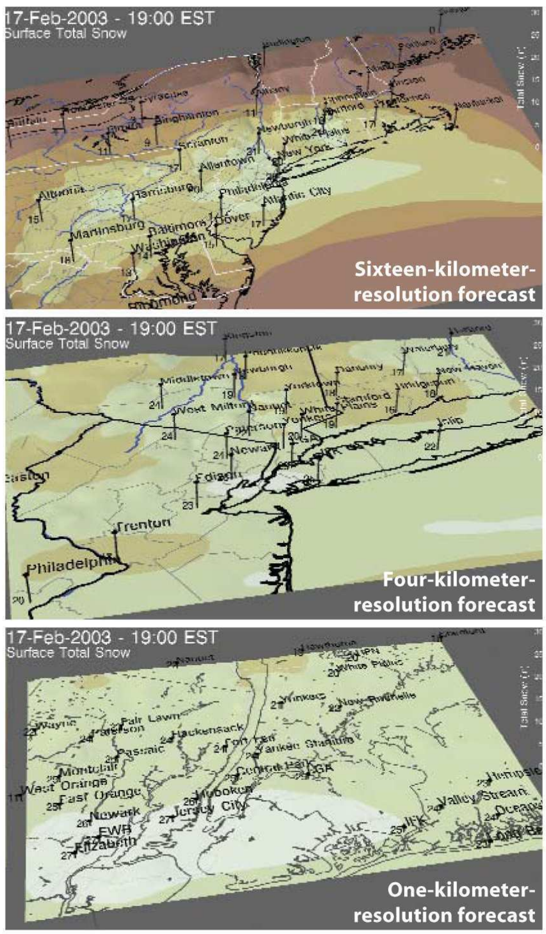
Digital Cyclone, for one, is capitalizing on Penn State's success. The company provides forecasts for a number of metropolitan U.S. areas, using a single PC to turn out a weather prediction for a particular city. The forecasts are twice as



Lighting the way: Stephen Marriott of Houston's CenterPoint Energy consults a high-resolution forecast map while head line mechanic William Shackleford inspects electric lines. Meteorlogix makes such maps accessible from laptop computers or handheld devices (opposite).
PHOTOGRAPH BY ROCKY KNETEN

frequent as those coming from the National Weather Service and cover a smaller area; that is, they run every three hours and have a resolution of six kilometers within about a 120-kilometer radius of the city.

Customers of Digital Cyclone can access the information from a Web site. By keying in their locations, they can get weather maps centered on their towns, complete with radar images and projected storm tracks. But the real value of Digital Cyclone's service, says Douglas, is that people can acquire the information from their Internet-enabled mobile phones. Later this year, those same phones will emit audible alerts sent out by the company and tailored to people's needs. And at a time when more and more mobile phones are equipped with Global Positioning Satellite software and signal receivers that provide information about their geographical location, Digital Cyclone is developing software—expected to become available in the next few years—that would use GPS data to offer high-resolution weather-forecasting maps automatically centered on the phone's location.



On the Business Front

Having personalized alerts beamed to your handheld device might seem the ultimate in weather awareness automation. But businesses also need detailed forecasts, and some weather providers are already integrating the information directly into the computers of their large industrial customers. A leader in this new field of "weather-enabled" operations is Meteorlogix in Minneapolis. The company uses satellite communications to relay customized weather updates directly into a client's operational computer system; preprogrammed to work with Meteorlogix's alerts, the computer system recognizes which operations are affected by the weather and then takes appropriate action.

Consider how Meteorlogix works with Union Pacific Railroad, the largest railroad in the United States, with more than 10,000 locomotives. High winds pose a safety hazard for railroads and can even flip a freight train off the tracks. Meteorlogix now constantly monitors the weather over all locations where the company has tracks and provides forecasts with a resolution down to one kilometer. The software pinpoints hazards and avoids false alarms by analyzing high-resolution radar to determine, in finer detail than the National Weather Service, the movement of different sections of storms. In this way, the path of the most intense parts of a storm can be identified locally. If high winds are in the forecast for Union Pacific, an alert is sent to the company's national dispatch center in Omaha, NE. Union Pacific responds by stopping or diverting trains. If Meteorlogix's computers don't receive confirmation within a few minutes that the alert has triggered a response, the computers automatically notify Union Pacific management.

The electric-power industry is also taking advantage of this type of automated weather forecasting. CenterPoint Energy in Houston, for one, uses Meteorlogix to help maintain electric service for 1.8 million people living in a 13,000-square-kilometer area. The Houston area is particularly prone to unpredictable storms; in 2002, high winds and lightning strikes from 13 severe storms left more than one million people without power. Operation supervisor Stephen Marriott, whose team is charged with restoring service during outages, now relies on a central monitoring station—which began using advanced weather-forecasting technology, including Meteorlogix, just last year—to enable it to foresee trouble. A technician at the station loads staffing details and the high-resolution weather information into the company's operational-system software. Staff members then manage the distribution of crews based on the system's recommendations. The crews are contacted by beeper, and each truck contains a mobile data system, complete with laptop and weather-imaging software that can track storm changes in real time. With the new technology, Marriott's team has been able to anticipate areas likely to be hit by the most intense parts of a storm and then respond quickly.

"Prior to 2002, the field people reported to us as storms developed," he says. "We more or less let the weather hit, and then we responded. It was backwards." Since incorporating the weather-forecasting technology into its operations, says Marriott, his team is responding better and working more efficiently. It now takes 38 people to do the same job it previously took 68 to do. They have also reduced the average outage time from 48 hours to as few as 16.

Sensing Rain

As computers become faster and cheaper and weather observation instruments improve, researchers promise even higher-resolution forecasts. In two or three years, some predict, resolutions will drop down to one kilometer. Getting there, however, will be an uphill battle. The first problem is the huge increase in computing power necessary to account for the additional variables of weather on such a small scale. "The topography of the local terrain, the presence of bodies of water, vegetation, cloud formation—all this has to be taken into account," says Joel Myers, founder and president of AccuWeather.

COURTESY OF IBM

Tower of power: Six weather-monitoring stations, like this one in Fishkill, NY, collect data to help improve IBM's Deep Thunder system, which produces forecasts at three different resolutions (opposite).
PHOTOGRAPH BY JAN STALLER

In fact, going down to one kilometer from four kilometers requires about 16 times the number-crunching muscle.

Despite the heavy computational price, Lloyd Treinish and his colleagues at IBM's Yorktown Heights, NY, research facility are working on one-kilometer-resolution weather forecasts. The so-called Deep Thunder project is part of a larger IBM effort known as Deep Computing, which is concerned with analyzing large amounts of data and solving complex computational problems. Like many companies working in the area of high-resolution weather forecasting, IBM foresees business opportunities in providing better prediction models to weather-sensitive companies. Treinish and his team have modified a standard regional model, developed at Colorado State University, and adapted it to the terrain, wind flow, and ocean-driven moisture patterns of the New York area. They use data received from the National Weather Service and then verify their forecasts using nearby weather stations—even one installed in Fishkill, NY. Later this year, IBM will install five more stations at its facilities in southeastern New York to help further fine-tune the models. Deep Thunder generates an updated 24-hour forecast two to four times a day, which requires almost two hours of computer time per forecast.

The modified model has proven its worth several times—as when it recognized the severity of a February 2003 blizzard some nine hours before the Weather Service. Treinish attributes the model's accuracy to its fine resolution, which in addition to providing a more detailed look at local weather often leads to better forecasts for an entire region. "By getting at the physics behind smaller-scale weather events, you can get a better picture of what's going on with larger-scale events like storms," he says.

Treinish even talks of getting down to 500-meter resolution in the future, though he points out it would require modeling wind turbulence around New York City's tall buildings—and it would demand about 100 times as much number crunching. "But that's not an unheard-of increase in computing power, if you're willing to wait a few years," he says.

"INSTEAD OF SAYING THERE'S A CHANCE OF RAIN TODAY, WE COULD SAY THERE'S A 20 PERCENT CHANCE OF RAIN BETWEEN 10 A.M. AND NOON AND A 40 PERCENT CHANCE BETWEEN NOON AND 2 P.M."

Such accurate, high-resolution weather forecasts depend on models that are regularly recalibrated by comparing their predictions against actual observed weather. But trying to tell whether or not forecasts are improving is harder than it sounds, because the differences can be subtle and complicated: perhaps wind speed predictions are getting a bit more accurate, while temperature predictions are getting a bit worse. David Stensrud of the National Oceanic and Atmospheric Administration's Severe Storm Laboratory in Norman, OK, notes that improving the models is slow going. "These models are so complicated that if you can correct for one problem you can easily cause another one," Stensrud says. "You have to run the new model over a large number of cases to check it, and that makes it a huge, labor-intensive effort."

And of course, a forecasting model is only as good as the instruments feeding it data. Eventually, meteorologists may be able to access finely detailed weather data from vast networks of sensors spaced just tens of meters apart over many parts of the country. A group led by Deborah Estrin, a computer scientist and director of the Center for Embedded Networked Sensing at the University of California, Los Angeles, is already embedding wireless sensor networks designed to monitor microclimate data—including, eventually, carbon dioxide levels—around small patches of trees and plants. "We want to explore the relationship between monitoring weather on a regional scale and on a microscale," she says.

Gathering such specific data may be in our future, but is it practical? "Putting out forecasts at the level of city blocks definitely makes it seem as if the forecasts are more precise," says Craig Edwards, chief meteorologist with the Minneapolis office of the National Weather Service. "But the forecasts for one block would probably be the same as for other blocks." There's also a trade-off between resolution and how far into the future a model can make accurate predictions, says Young, because of how quickly small-scale weather phenomena change. "Today's high-resolution forecasts are useful for a day or so," he says. "We're rapidly heading to resolutions that won't buy you anything beyond six hours."

Regardless of the new technology's utility, meteorologists will be able to show off more of it in their forecasts as the public gets comfortable with weather jargon and maps. "The weather IQ of the public has increased tremendously over the last 10 years," says AccuWeather's Myers. "Instead of saying there's a chance of rain today, we could say there's a 20 percent chance of rain between 10:00 A.M. and noon, a 40 percent chance between noon and 2:00 P.M., and a 20 percent chance after that. That's the sort of information you could use to schedule your golf game." TR

Others in High-Resolution Forecasting

COMPANY	GRID RESOLUTION	SERVICE
Meteo Consult (Wageningen, Netherlands)	Site-specific, based on location of weather stations	Weather maps and satellite and radar images delivered to Web-enabled mobile phones
MyWeather (Madison, WI)	110 meters	Text message forecasts sent to alphanumeric pagers and mobile phones
AWS Convergence Technologies (Gaithersburg, MD)	Site-specific, based on location of proprietary weather stations	Web-based application that provides forecasts for customers in the energy industry
Weather Services International (Billerica, MA)	Eight to 10 kilometers; point-specific forecasts	Weather maps and satellite and radar images delivered to people working in the media, energy, marine, and aviation industries (pilots can receive data in-flight on personal digital assistants)


X
LIMIT

YOU bought it.

A LEADING THINKER ON THE IRONIES OF TECHNOLOGY ARGUES THAT MACHINES MEANT TO LIBERATE US ARE INSTEAD PUTTING CONSUMERS IN A STRAITJACKET—AND STIFLING VITAL INNOVATION IN THE PROCESS.

ESSAY BY EDWARD TENNER • ILLUSTRATIONS BY STUART BRADFORD

WHO controls it?

The personal-computing revolution began with a promise: after decades of submission to centralized mainframes, ordinary users were now in control. Buttoned-up IBM loosened its collar, opened its new PC to accommodate hardware and software from a variety of suppliers, and even bought its operating system from a couple of Harvard University dropouts. To reinforce this message, IBM chose as its marketing emblem a look-alike of Charlie Chaplin—timeless hero of the harried underdog. It was a clever choice, and not inappropriate: the PC and other machines like it really did confer upon users a degree of control over information never before available. Twenty years later, technology industries are still promising us autonomy and independence.

But that promise is falling flat. Asserting an unprecedented degree of control over their goods, even once they are in the customers' hands, technology producers are moving to circumscribe the freedom that technology users have long taken for granted. The same powerful trends that have brought leaps in performance—ubiquitous microprocessors, cheap digital storage, and virtually free data transmission—are making possible new ways for technology makers to control users' behavior. These developments reek more of Big Brother than the Little Tramp.

It's not that companies have ill intent. Manufacturers are offering hardware and code they claim will release the full potential of information technology: promoting creativity and productivity while making computing and the Internet secure and reliable at last. Their products address real problems—from brand counterfeiting and piracy, which cost billions, to malfunctioning equipment. But despite the benign intent, some features built into new generations of devices, like the Greek infiltrators in the belly of the Trojan horse, provide openings for intrusion and even conquest. Call it the Trojan mouse.

Measures to control behavior can depend on either accountability or incapacitation. Think of automotive traffic control. Until recently, most communities tried to control speeding with radar-equipped patrol cars. More recently, some towns have shifted to a strategy of incapacitation: they are making speeding physically difficult with increasing use of "traffic-calming" devices such as speed bumps. Police radar is a technology of accountability; it needs the courts to be effective and can be defeated at least some of the time by sensitive detectors. Traffic-calming structures, by contrast, are technologies of incapacitation: they limit passively what people can do with their vehicles.

Technology makers increasingly prefer incapacitation as a strategy of control. The software industry, for example, once used a double standard for enforcing its licenses: companies vigorously regulated software usage by commercial establishments while pretty much letting individual consumers do as they pleased. But as the distinction between home and office blurs, consumers now find themselves wrestling with the sort of constraints once intended mainly for corporate users. Microsoft is leading the way by beginning to license its Windows operating system for household use in much the way it deals with businesses: each machine must have its own paid upgrade to the next version. Users do have the right to continue running older versions of Windows, but they may find that new programs they want or need run only on the latest release. The result is "forced migration," to use a stark metaphor dating from the mainframe era. Other technology and entertainment companies are also cracking down through incapacitation. Instead of paying more patent and copyright lawyers to take alleged infringers to court, they are modifying their products so that the user is physically barred from using them in unsanctioned ways. The traffic cop is giving way to the speed bump.

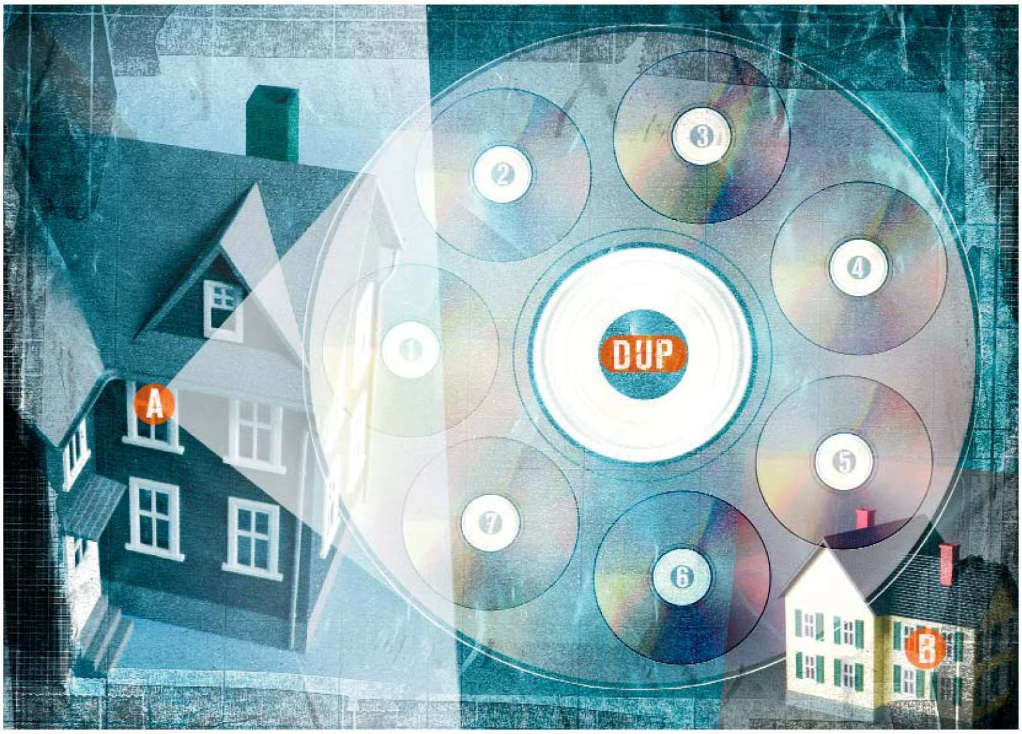
Information Lockdown

In the early days of the PC software industry, elaborate anticopying systems blocked users from duplicating programs for use by friends or colleagues. By the 1990s, consumer resistance had restricted copy protection to niche products such as computer-assisted-design programs. But now, companies are reimposing such limits. Here again, technology producers are displaying a taste for incapacitation.

Yes, copyright owners have tried using accountability—they took Napster to court and brought the file-sharing service down with a lawsuit. But that was a victory in one battle of what has become a widening war; a new file-sharing network seems to rise from the ashes of each defeated one. Individual songs and entire movies are now routinely available on the Web weeks before their official release. While the music industry is beginning to introduce its own download sites online and, soon, in retail stores, it is also alarmed by peer-to-peer exchange among friends. Soon, even entry level personal computers will have the capability to record CDs and DVDs, and enough disk space for hours of music and video. The consumer, in other words, is becoming a low-cost rival manufacturer and, through Internet file sharing, an essentially zero-cost rival distributor. The strategy of accountability, it seems, is losing the war.

Companies have already begun to limit movements of data. Sony, a leading audio and video company and copyright owner, may be offering a preview of controls to come. Some of its computers already use proprietary software to encrypt digital music, limiting the number of times a song can be downloaded ("checked out," in Sony's parlance) to an external device. After three downloads, a song must be "checked in" to the original device before it can be checked out again. While the aim is protection of copyrighted material, the program makes it difficult to duplicate any CD at all—including one that contains music created and recorded by the owner.

MEASURES TO CONTROL BEHAVIOR CAN DEPEND EITHER ON ACCOUNTABILITY (THINK TRAFFIC COPS) OR INCAPACITATION (SPEED BUMPS). MAKERS OF TECHNOLOGY ARE TURNING MORE AND MORE TO THE STRATEGY OF INCAPACITATION.



Such schemes will of course have little effect against the greatest economic threats to the copyright holders: the pirate factories of eastern Europe and Asia. These illicit operations can pay technical experts to defeat protection, or bribe insiders for unprotected copies of source material. Whether intentionally or not, therefore, Sony is targeting the controls at the less serious losses from sharing among friends.

Why should a legitimate owner of a CD or DVD object to such copy protection? These schemes do, after all, permit backups and second copies for use in other machines, such as portable or automobile CD players. But the controls can also degrade the quality of the product. Even some electrical engineers who believe that sophisticated copy protection is undetectable to most listeners acknowledge that because music and videos already make use of data compression algorithms that take advantage of the limits of human senses, a few people with especially discerning ears may indeed be able to tell the difference. Moreover, copy control often works by weakening the error correction schemes in the stored data—an alteration that may wash out subtleties of performance or make discs less scratch resistant.

Last October, *Audio Revolution* magazine reported that DVD players constructed without the normally mandated series of internal conversions between digital and analog formats—circuits included by industry agreement purely to foil piracy—produce "stunning" images compared to those from conventional players. The British organization Campaign for Digital Rights has denounced copy protection as an unacceptably blunt weapon against piracy: determined outlaws can still find computers that will allow the CDs to be ripped for MP3s, while honest consumers receive what many audio and video enthusiasts consider musically compromised products.

Despite the complaints, past experience has shown that what technology *can* control, the law *will* control—or at least try to. That's exactly what has happened here, as constraints on data copying draw strength and legitimacy from the force of the Digital Millennium Copyright Act of 1998. This legislation provides harsh penalties not only for piracy but also for publicizing ways to circumvent security. So far, however, the law appears not to have slowed the diffusion of control-evading techniques: the anarchical impulse of technology users is not easily suppressed.

Security vs. Freedom

In the most thorough form of incapacitation, technology makers are building their products to resist any form of alteration once they leave the factory. The paradox here is that while many technology users resent such control, they also need it. A computer network that is truly open, for example, is also dangerously vulnerable to attack by viruses.

Not surprisingly, these days the computer industry is giving higher priority to security than openness. Take, for example, the controversial Microsoft project originally known as Palladium and recently renamed Next-Generation Secure Computing Base for Windows. This effort involves the development of a set of secure features for a new generation of computers. The goal: let users such as banks communicate in ways that prevent disclosure of information to unauthorized persons, using stronger hardware as well as software protection. The system would protect the privacy of medical and financial data far more effectively than today's security software, and Microsoft insists that it will not restrict the rights of most computer owners; machines will be shipped with the new capabilities turned off.

A computer built on the new specification could run existing software like any other. But the Secure Computing Base could give Microsoft or other vendors the power to disable third-party software on their customers' computers, if they believe it circumvents rights management. Vendors could also detect and disable user hardware modifications that, as judge, jury, and executioner, they deem a threat to the security of their programs. As evidence of this intent, critics point to phrases in the user license agreements of Microsoft's Windows Media Player that seem to allow the program's security updates to disable other programs. "The keys will be kept in tamper-resistant hardware rather than being hidden in software," contends Ross Anderson, a University of Cambridge computer scientist. "There will be lots of bugs and workarounds that people discover, but eventually they will get fixed up, and it will be progressively harder to break."

Paul England, a software architect at Microsoft familiar with the system, considers such fears unwarranted. There is, he says, "no a priori remote control" that it will impose or let others impose on a user's applications. Copyright owners would not, he insists, be able to use the system to inactivate other programs that could capture their data and store it in different file formats.

This blanket of security can smother as well as protect. Web businesses and software vendors will have the option of offering their products only to "trusted" machines—that is, those in which the protection system has been activated. Most content

companies would probably begin to restrict compatibility to trusted machines. Downloading a magazine article or a song, for example, might require a machine in which the Microsoft technology was present and activated.

Such measures can prevent hackers and unethical companies from stealing personal information and hijacking personal machines for nefarious purposes. But tamperproofing technology also allows companies, while flying the banner of fighting piracy, to take steps that degrade the performance that law-abiding consumers get from their computers.

Critics argue that Microsoft's Secure Computing Base comes at too high a price. Princeton computer scientist Edward W. Felten warns that if technology vendors "exploit Palladium fully to restrict access to copyrighted works, education and research will suffer." Scientists, he points out, must be able to inspect and modify electronic technology, just as automotive engineers and designers must be able to take vehicles apart and tweak components. Mark Granovetter, a professor of sociology at Stanford University, says that a massive public backlash would prevent Microsoft from implementing the Secure Computing Base.

Others, however, are more pessimistic. Jonathan Zittrain, a professor of information law at Harvard, foresees the introduction of "closed, appliance-like devices as substitutes for the general PC." Such appliances would be more reliable than PCs but would offer their owners less control. Zittrain fears the end of what will be seen, in retrospect, as a fleeting era of computer freedom. "A diverse and vibrant community of independent software developers and vendors," he says, may have been "a transitory phenomenon of the 1980s and 1990s."

If Zittrain's prophecy proves correct, the locked-down landscape of technology will disappoint its architects. First, incapacitation will not eliminate the costs of accountability but rather shift them. A regime of constraints depends on laws banning technologies that would defeat or circumvent the control schemes, and those bans will need to be enforced. Second, protection may degrade data, if only subtly, and introduce bugs that may stain a brand's reputation and compromise its market share.

THE TAMPERPROOFING THAT SOME TECHNOLOGY COMPANIES ARE NOW PUTTING IN PLACE THREATENS A TRADITION OF USER-CENTERED INNOVATION. INCAPACITATING DESIGNS WILL SLAM THE DOOR ON THESE VITAL SUPERTINKERERS.

Indeed, the kinds of tamperproofing now being put in place threaten the individual tinkering upon which so much innovation is based. They would deprive people of their longstanding right to improve on products they lawfully own—even when they are not violating copyrights or creating hazards. Such user-centered innovation has a long history in the United States. Henry Ford's Model T and tractor, for example, were made for resourceful country people who constantly found new uses for them: once the drive axle was lifted and a wheel removed, the hub could drive tools and farm equipment. It was a mini power station on wheels, its variations and applications limited only by the user's imagination.

Some contend that the freedom users have to modify a system and its software is worth the risk. As John Gilmore, a cofounder of the Electronic Frontier Foundation, a Washington, DC-based civil-liberties organization, has written, "Be very glad that your PC is insecure—it means that after you buy it, you can break into it and install what software you want. What *you* want, not what Sony or Warner or AOL wants."

The Cost of Control

Legislation now pending would make tamperproofing the law of the land. Senator Fritz Hollings (D-South Carolina) has introduced a bill that would require all electronic devices—from computers to Furby toys—to have built into them some form of rights-management or security software that would limit users' rights to inspect and modify them. According to Hollings's office, the measure is intended to prod the electronics and media industries to come to an agreement on security standards.

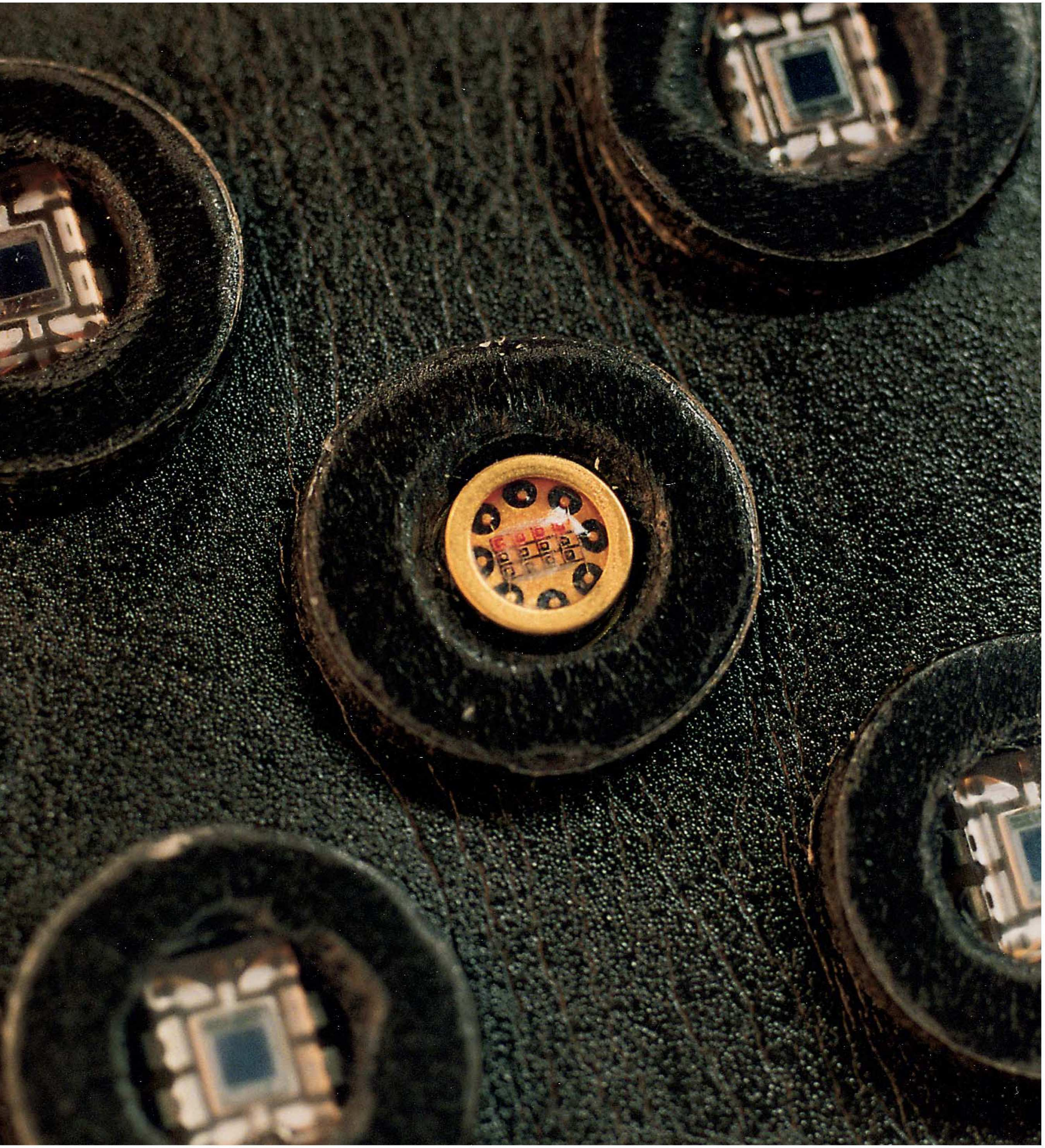
Some information technology experts remain sanguine. Even if the Hollings bill becomes law, they contend, competition and market pressures will preserve people's freedom to modify the technological products they buy.

Most seriously, forms of control that work through incapacitation will undermine the chaotic, dynamic society that made the personal-computing revolution possible in the first place. Powerless against determined pirates, they would strike hardest at creative customers, such as the chip-modifying fans who have breathed new life into moribund computer games—the very people whose ideas could help develop new generations of lucrative products. As MIT management professor Eric von Hippel wrote in 2001 in the *Sloan Management Review*, "innovations that only a few leaders use today may be in general demand tomorrow"—especially, he says, if early adopters "have a chance to innovate, to learn by doing, and to develop the general utility of their innovations." Incapacitating designs will slam the door in the faces of these vital supertinkerers.

Incapacitation would also limit the academic training of companies' future technical staff. Freedom to tinker—defined by Felten as "your freedom to understand, discuss, repair, and modify the technological devices that you own"—benefits technology industries most of all. Even the film industry needs young people who have had free access to the nuts and bolts of digital graphics and special effects, and I'll bet that Microsoft doesn't make its young Xbox game-programming recruits sign an affidavit that they have never violated an end-user license agreement. New hardware security is manifestly a good idea for servers with sensitive information. There is a good case for new levels of protection, like the Microsoft scheme, for these vulnerable sites. But if they extend incapacitation too far, the builders of the Trojan mouse may find themselves caught in their own trap. TR

Edward Tenner is author of Why Things Bite Back: Technology and the Revenge of Unintended Consequences *and the forthcoming* Our Own Devices: The Past and Future of Body Technology *(Knopf)*.


VIOLATE
VICTOR
VICTOR

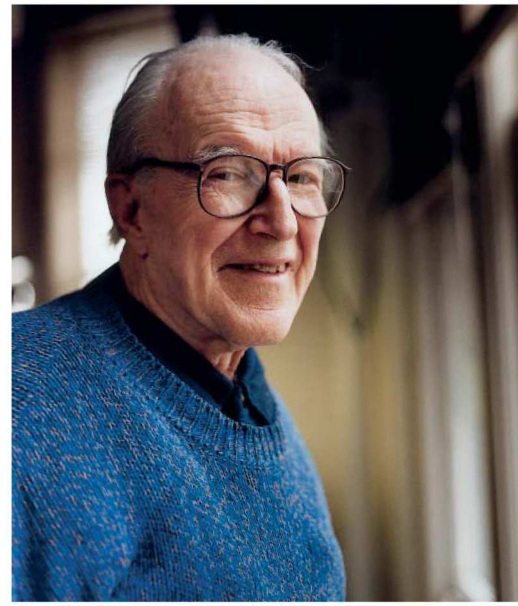


DEMO

The Deceit Detector

You didn't lie—your prefrontal cortex did. And **Britton Chance** is developing infrared-based brain imaging to catch it in action.

Photographs by James Wasserman

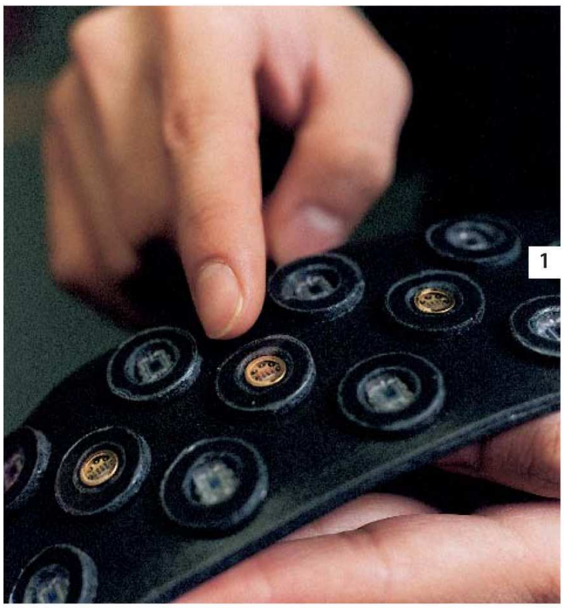


Truth seeker: Britton Chance's device (left) uses gold-colored infrared-light emitters surrounded by detectors that measure light reflected from the prefrontal cortex.

FORGET THE ELEVATED PULSES, sweaty palms, and respiration changes scrutinized by conventional lie detector tests. There's a more direct and, in theory at least, accurate way to measure deceit: track the flow of blood where the lie is born. Lying requires an extra bit of thought, which pulls more blood into a swath of the brain just beneath the forehead. These flows can be tracked optically. And biophysicist Britton Chance—who 60 years ago was part of the wartime research team that developed radar at MIT's Radiation Laboratory—is pioneering technology that can literally see a lie as you speak it. He believes the method is better than conventional tests because the flows can't be suppressed and are less likely to have been caused by the stress of test-taking.

Chance's device uses infrared light, which penetrates tissue. Some of the light is reflected, but since blood selectively absorbs it, increases in blood levels reduce reflection. Precise spacing of light emitters and detectors on a headband allows researchers to gauge the depth at which most of the light is reflected; the target is the prefrontal cortex. "That's where your decision-making goes on, and where most of your societal inhibitions reside—if you have any," Chance says. "That was what we wanted to study. Knowledge and inhibition. Fear and deceit." Chance is developing the technology not only for studying the cortex in action—for lie detection and cognition studies—but for other applications like breast cancer screening. In his University of Pennsylvania lab, Chance, 89, showed *Technology Review* senior editor David Talbot how to use light to find truth.

1. The deceit detector's critical parts are light emitters and detectors embedded in a headband. Four gold-colored light sources are attached to the middle of the headband. Each source has two infrared light-emitting diodes (LEDs) that produce different wavelengths; one wavelength is absorbed more by oxygenated blood, the other more by deoxygenated blood. These emitters are flanked by 10 silicon light detectors that sense infrared light reflected back from the brain. "The detectors," Chance says, "are just far enough away so that the light that gets to them is light that has gone through the



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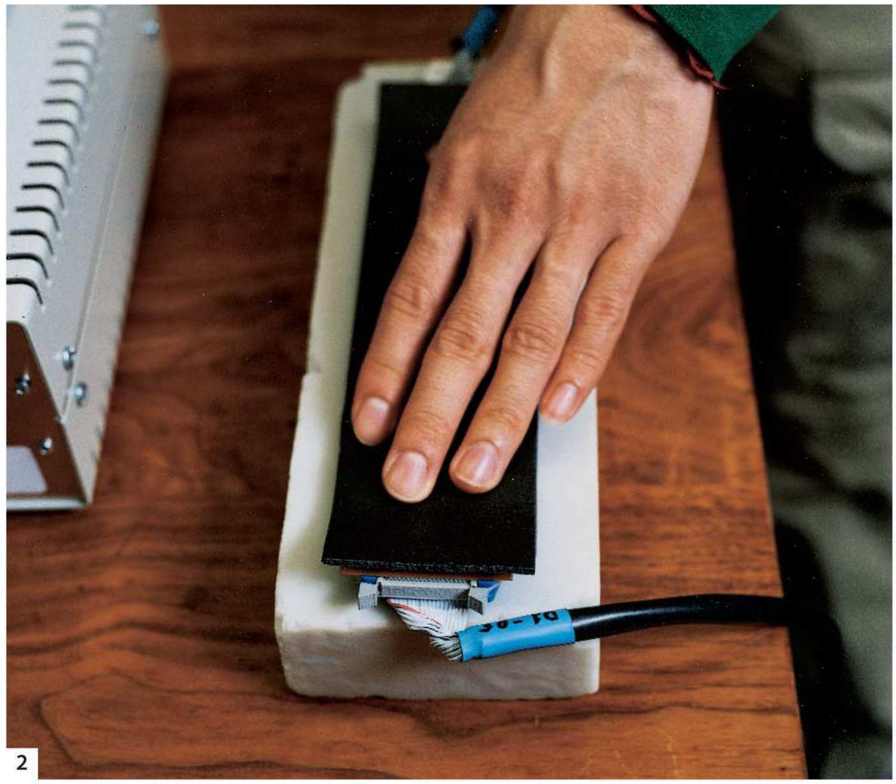

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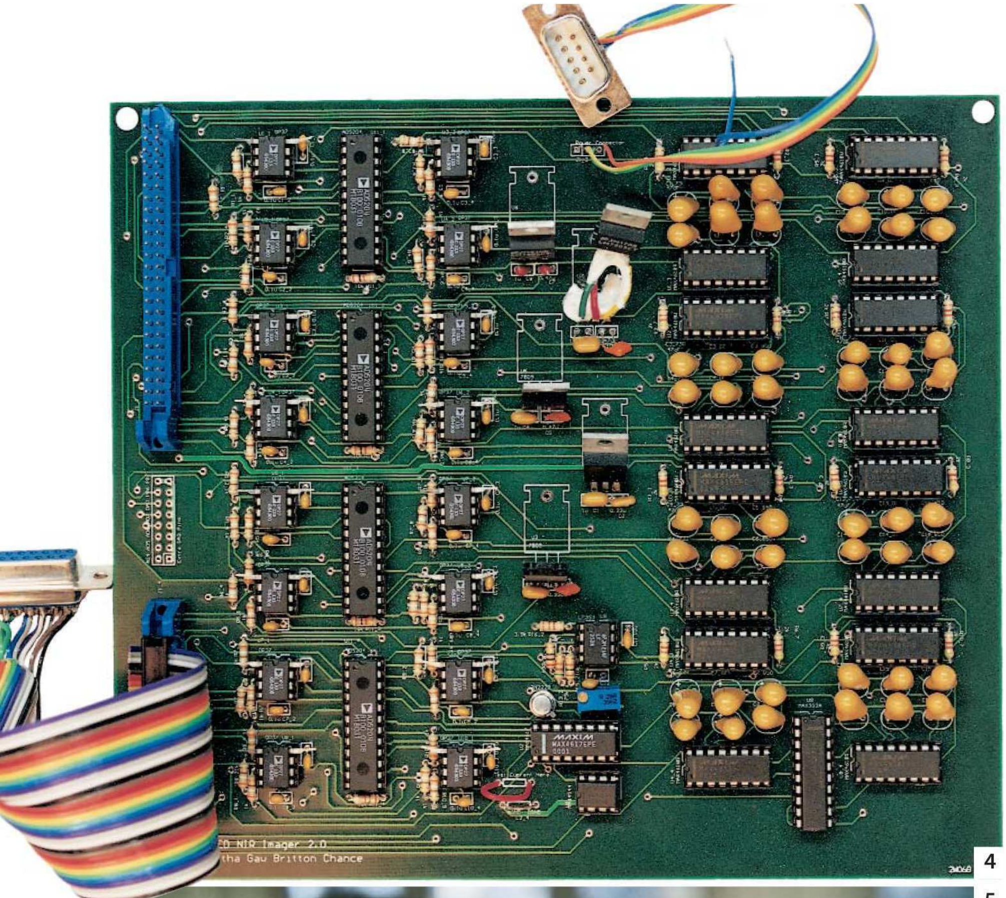
skin, the skull, and into the brain cortex"—and then back out. A computer can analyze the reflected light signals to determine changes in total blood volume and in level of oxygenation; those are "the two signals that change dramatically when you start to think, when you start to solve a problem, and when you start to deceive somebody," Chance says.

2-3. Before the headband can be used, it must be calibrated. Postdoc Simon Wen presses it into a rubbery block, made of silicone and titanium oxide, that has optical properties similar to a human brain's. Wen checks for uniform readings from the 10 sensors before placing the device on the head of his colleague Barry John-Chuan, who has volunteered to respond to a series of personal questions. For the purposes of the demonstration, after some questions he's instructed to lie; after others, he's told to tell the truth.



4. The optical devices now pressed against John-Chuan's head are governed by a circuit board, shown here out of its box. The board controls the 10-millisecond light bursts from the four LED emitters, and also processes signals coming back from the 10 detectors. Some detectors do double duty, picking up signals from two emitters on an alternating basis, so the final output is 16 signals from 10 detectors. "The board cleans them up," Chance says. "They have to be amplified and integrated." Once this job is done, the signals move on to a laptop computer, where software makes sense of them.

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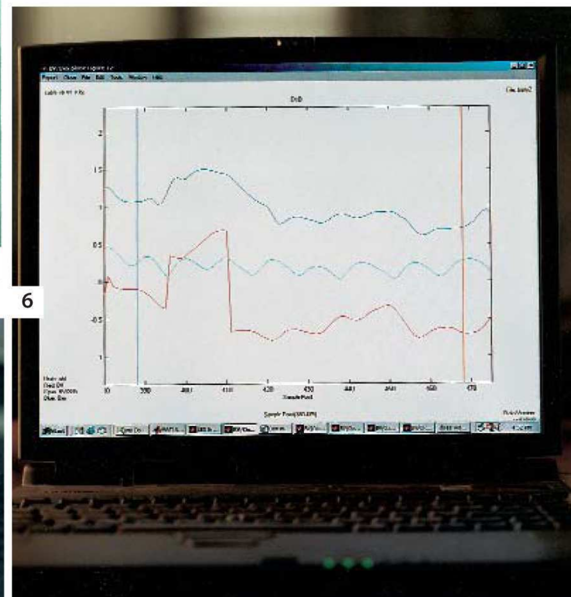
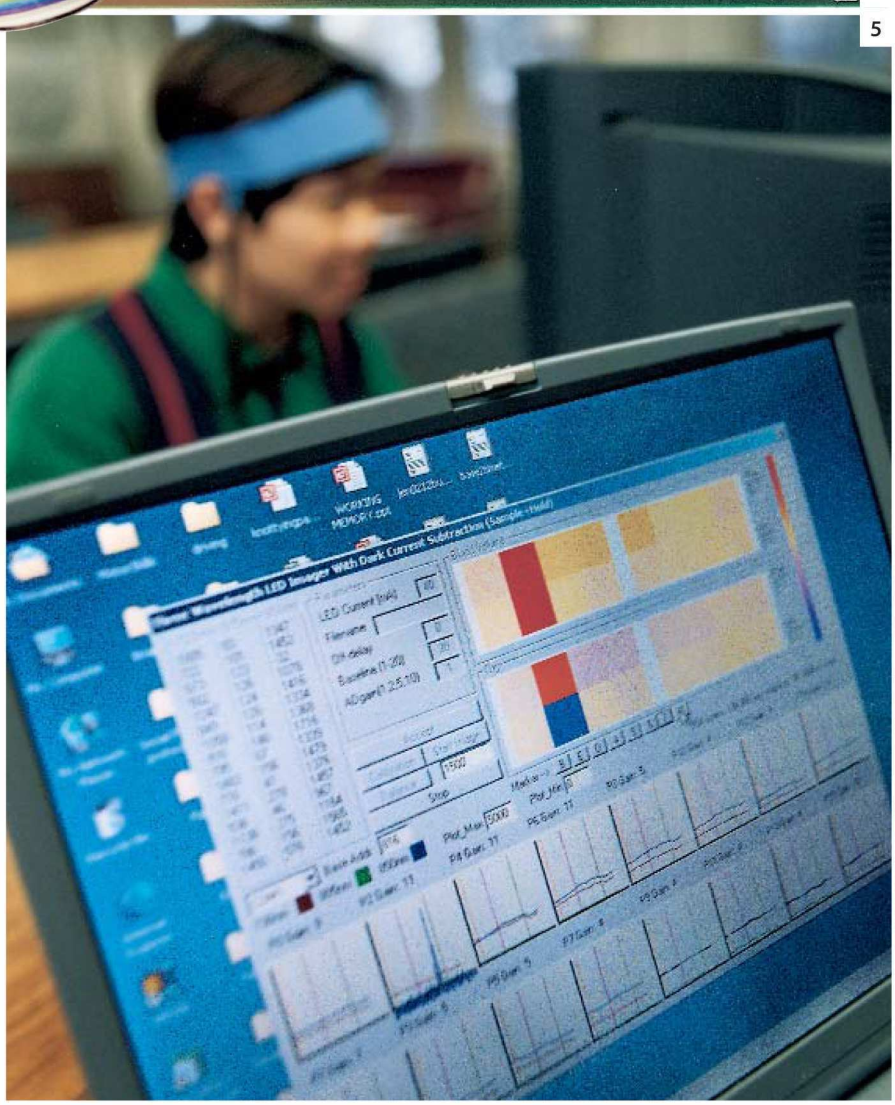




5. The results of these cleaned-up signals now appear on a laptop-computer display. The top two rows show blood volume levels; the bottom two rows show oxygenation levels. During deceit, shadings of all boxes tend to get redder as the prefrontal cortex concocts the lie.

6. With questioning done, it's time for a reality check. The changes in blood volume and oxygenation in John-Chuan's prefrontal cortex are displayed. A vertical line to the left of the screen marks the moment he was asked, "Have you ever gotten drunk?" Told to lie, he'd replied "No!" But the detectors showed an increase in blood levels (blue line) and in oxygen levels (red line). "When you've made the decision to lie, you may not know you've made the decision," Chance says with a grin. "But the brain has a signal that you don't know about." It's a signal that can't fool the deceit detector. TR

By Erika Jonietz | Photograph by Anne Hamersky

CLONING, STEM CELLS, AND MEDICINE'S FUTURE

Thomas B. Okarma

POSITION: President and CEO, Geron

ISSUE: Embryonic-stem-cell and cloning research. The U.S. political climate is proving inhospitable to biomedical research that could benefit millions, and other nations are jumping in to fill the void.

PERSONAL POINT OF IMPACT: Over 20 years of research to create commercial cell-based therapies.

TECHNOLOGY REVIEW: Human embryonic stem cells, primitive cells with the ability to form every type of tissue, could lead to effective treatments or even cures for ailments such as heart failure, Parkinson's disease, diabetes, and spinal-cord injury. But creating the cells requires destroying human embryos, a hugely controversial issue. How do you address that?

TOM OKARMA: These cells are derived from embryos created using in vitro fertilization that are donated under informed consent by couples who no longer need them to achieve pregnancy. For the couple, their choice is threefold: have the extra embryos stored frozen, forever; have them destroyed; or donate them for research. Our whole justification for trying to develop this field isn't that we don't have regard for the sensitive issues of creation of life. It's because in that unused embryo is the most incredible cell ever discovered, a cell that solves the technical, commercial, economic, and medical problems that have prevented cell therapy from making it in the past 20 years. The fact that one embryo produces untold billions of cells for thousands of patients' therapies is enormous ethical leverage. A master cell bank of embryonic stem cells can make enough dopamine-producing neurons for 10 million Parkinson's patients. That is beyond our wildest dreams, even three years ago!

TR: One argument you hear quite a lot is that experiments by academic researchers have shown that stem cells from adult tissues, such as bone marrow cells, can be transformed into all these cell types, too. So why use embryonic stem cells?

OKARMA: Well, first of all, no one has actually shown that. That is a misinterpretation of the data. With this kind of research, you're asking a cell that is naturally programmed, let's say, to make blood—to use the most commonly cited adult stem cell—and you're trying to turn it into a liver cell or a heart cell or a brain cell. These cells are not programmed to do that. So even if you are able to belt those cells over the head to make a half a percent of them morph into heart muscle cells or neurons, those cells are not making that transition in a scalable way. So you'll never be able to address the market with that kind of process. You're back to an individualized, case-by-case therapy, back to the old bone marrow transplant model.

TR: In 2001 President Bush limited federal funding for embryonic-stem-cell research to cell lines that existed before that time, with each line consisting of cells derived from a single embryo. What consequences has this had for the field?

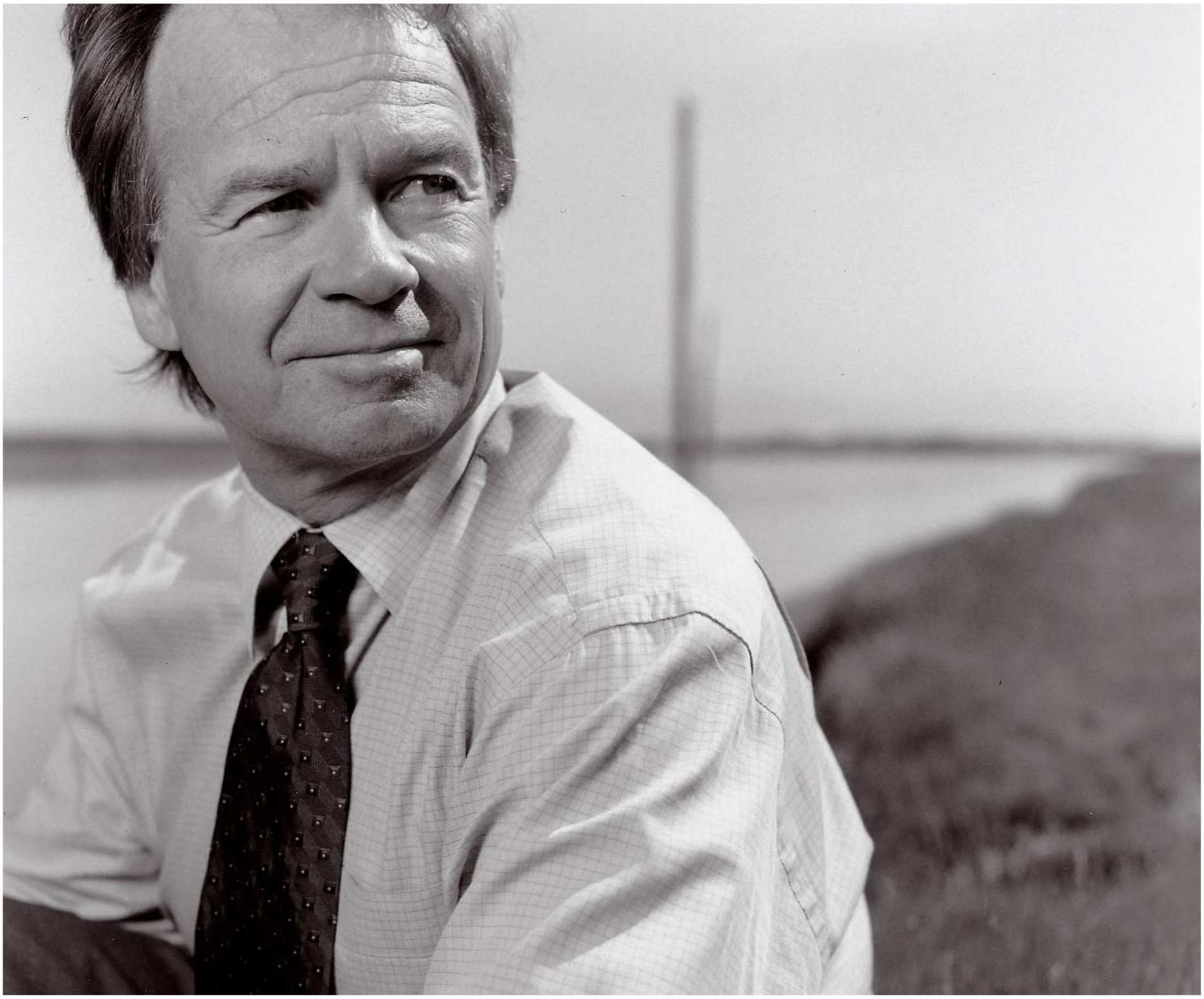
OKARMA: I'm not making the case that the Bush decision has stifled the research or prevented us from making progress, but it is shortsighted. For example, as far as we're aware, all of the lines in the world were derived by the initial patented process from the University of Wisconsin-Madison that involves culturing the early embryo on mouse feeder cells. The FDA [U.S. Food and Drug Administration] appropriately classifies all of these lines as xenogeneic—as if they came from a mouse—simply because they were cultured on mouse cells. We don't quibble with that classification. It's a problem, though, because when you try to put those cells into humans, the bar is higher. There's a theoretical possibility that mouse viruses could have jumped from the mouse cell into the human cell. So both the FDA and the research world want to produce cells in a slightly different way that would not ever utilize mouse feeder cells. And we are in the process of doing that. There's no question we will be successful in doing that. But once we are, because of the Bush decision, the National Institutes of Health cannot use those lines, because they were derived after the Bush decree. This is, to our mind, anti-intellectual. One branch of the government is saying no; another branch of the government—the FDA—is saying, make these lines safer.

TR: In February, the U.S. House of Representatives passed legislation that would ban all research into human nuclear transfer—the technology behind human cloning. But some scientists believe nuclear transfer offers a way to make stem cells that would be a perfect tissue match to the patient who needs them. How would this affect efforts to create therapies using embryonic stem cells?

OKARMA: The efficiency of making a stem cell line from an embryo made by nuclear transfer is vanishingly small, and you're going back to the case-by-case, individualized-therapy story again, with enormous costs. The whole idea is to make this therapy internationally available, broadly. Nuclear-transfer procedures just are never going to get us there.

There are, however, reasons why we are opposed to the current congressional mood of criminalizing and banning all nuclear-transfer research. Everybody's on the same page about not cloning people. There are many reasons not to do that. But there are valid reasons why we should be doing nuclear-transfer research. We know the sequence of the whole genome and are now in a position to start doing very intelligently the kind of genomic research that will lead to understanding how it is that my family history for disease X—let's say breast cancer—gets manifested. How do the genes that cause people in my family to have a high likelihood of developing breast cancer work in my cells?

There is no platform, biologically, to work that out, except embryonic stem cells. So you would do nuclear transfer



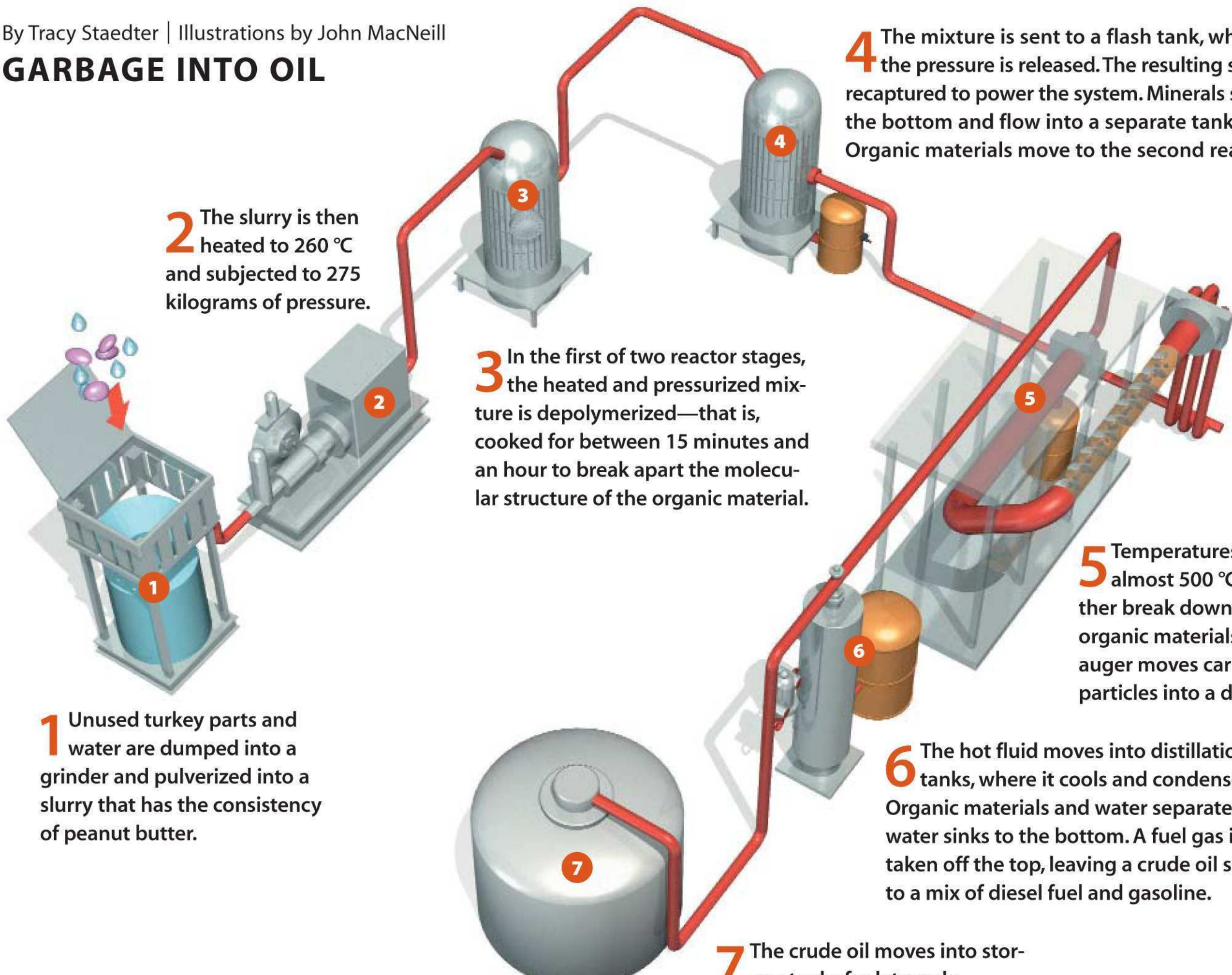
with my cells, which carry all those genes, and you'd make a stem cell line from me. Now you can make breast cells and study how my inherited predisposition for breast cancer is actually working to produce disease. It's the perfect platform to take the next step in genomic research, to make it real for patients. This is absolutely bona fide, important, potentially breakthrough research for people with these genetic diseases. Not just cancer: Tay-Sachs disease, sickle cell anemia, on and on and on. It's the most viable way to unravel how genetic disease is manifested in tissue that will lead directly to treatments. Now our House of Representatives, in their wisdom, want to criminalize that research.

TR: How would such a ban affect stem cell research?

OKARMA: It would be a huge chill. Now, is that going to result in 50,000 scientists leaving the country? Probably not. But what is happening is that other countries—Australia, Canada, Scandinavia, the U.K., Singapore, China—where the governments and academic institutions see an opportunity to leapfrog the United States, are pouring a lot of money into stem cell research, including nuclear transfer. It's not that they're ahead of us today. But it's very clear from my personal travels that they recognize how harmful our political debate is, and how potentially meaningful—even for the developing world—this therapy is, because it's scalable. It's not going to be prohibited from reaching the masses because it's sophisticated, Western medicine. And that's crucial to understanding why the developing world wants this technology, and why governments and academic institutions are pushing it. So what's happening is that Asia sends their brightest young folks over to the NIH for a half-dozen years of training, and normally those folks stay in this country. Now they're going back home, if they're in the field of embryonic stem cells, cell therapy, or nuclear transfer, because they're going back to an environment where they can practice what they've learned.

By Tracy Staedter | Illustrations by John MacNeill

GARBAGE INTO OIL



The recipe for making crude oil is relatively simple: combine the remains of ferns, jellyfish, and dinosaurs; cover with sediment; bury deep in the earth's crust; and apply pressure for millions of years—give or take an epoch. Or if you're pressed for time, run some turkey parts or used tires through the thermal process owned by Changing World Technologies of West Hempstead, NY. The system uses water, pressure, and heat to convert organic material into clean fuel gas, absorbent carbon (like that used in water filters), minerals for fertilizer, and a crude oil that is chemically similar to a mixture of diesel fuel and gasoline; this oil can be sold to refineries and converted into fuel. The system produces no polluting emissions, and the only by-product is water.

In April 2003, the first commercial thermo-depolymerization plant opened in Carthage, MO. Every day, the plant handles 200 tons of unused turkey parts produced by ConAgra's Butterball turkey plant. Such waste is now typically reprocessed into animal feed, but this practice may not be allowed much longer in the United States: Britain has already outlawed it in the wake of hoof-and-mouth and mad-cow disease outbreaks traced to reconstituted animal feed.

The first stage of the thermal process has been around since the 1960s as a way to convert organic waste into hydrocarbon liquids. But the process has been inefficient, says Changing World chief technology officer Terry Adams, because it typically employs a single reactor both to heat the organic matter and to convert it into oil. That creates nonuniform heating, which breaks down molecules unevenly and results in a low-grade oil. Changing World uses two main reactors that heat and pressurize much more efficiently. And the system handles not only turkey offal but tires, plastics, sludge, municipal waste, paper, and livestock remains—expanding its potential for widespread use. "They have certainly produced the products they've claimed at a smaller scale," says MIT chemical engineer Jefferson Tester, who visited a pilot plant in Philadelphia and is intrigued by the larger-scale possibilities. Mother Nature can definitely transform the same products into usable fuel; you'd just have to wait a little longer. TR

For an animated version of this illustration, go to www.technologyreview.com/visualize/.

SOURCE: TERRY ADAMS, CHANGING WORLD TECHNOLOGIES

OPTICAL breakthrough

Get a closer look... 80 times closer with SuperZoom compact binoculars.

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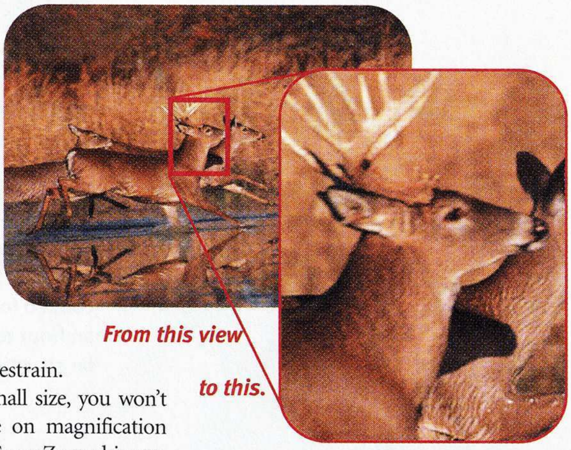

Are you tired of lugging around bulky binoculars on hikes or to sports events? Are your current binoculars too big to fit in your purse for the theater? Have you just skipped on buying binoculars because they are too expensive?

where or when you may want them to take a closer look at the natural world. With excellent zoom capabilities, they clear up distant objects and prevent eyestrain.

Even with their small size, you won't have to compromise on magnification and clarity. The SuperZoom binoculars feature high performance prisms and ruby coated lenses that provide unsurpassed infrared and ultra-violet protection. The coated lenses were developed using expert optic technology to produce exceptionally sharp, high-contrast images. Our binoculars have the capacity to allow you to view objects at 20x magnification and then zoom-in for pinpoint accuracy with 80x power. The center focus knob and independent right diopter adjustment offers maximum focusing capability, all without ever losing sight of the object you are viewing. With its one-touch zoom lever and sure grip finish on the body, you'll never miss seeing the action clearly again with our binoculars. The binoculars also come with a tripod adapter for ultra-still viewing. The designers thought of everything. You can even roll down the comfort eyecups so you can view through your binoculars *while wearing sunglasses.* Complete with protective case with belt loop and a worry-free neck strap, you'll take them everywhere.

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- **Compact-about half the size of most binoculars**
- **Great for sporting events, bird watching, races, air shows and more.**
- **Can be used with sunglasses**
- **Only 12.5 oz**
- **Affordable**

Binoculars are always useful if you're a bird watcher or sports enthusiast, but many for sale are big, bulky and lack any impressive features despite their high prices.

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If weight, size, eyestrain, or risk of loss are preventing you from taking your binoculars with you when you want them, Carson SuperZoom compact binoculars are the answer. And, with this special direct offer, they're an exceptional value you just can't miss. They come with the manufacturer's lifetime limited warranty and our 30-day money-back guarantee; if you're not completely satisfied, simply return the binoculars for the full purchase price, no questions asked.

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A PAINFUL IP RULING

I have done my share of griping about the deluge of overly broad intellectual-property claims pouring out of the U.S. Patent and Trademark Office. So I suppose I should cheer when the courts try to block this stream. But this spring, a Hoover Dam of a ruling—in a patent case involving broad ownership rights to the latest generation of painkillers—raises more painful questions about our patent system than it resolves.

The case pits the University of Rochester against the drugmakers Pfizer and Pharmacia. The University of Rochester claims a broad patent on the underlying research for the insanely lucrative painkiller medications called cox-2 inhibitors—including bestselling Celebrex, made by Pharmacia. Pfizer, which is in the process of buying out Pharmacia, claims that it developed the drug independently and therefore shouldn't have to pay royalties to the university.

The stakes could hardly be higher. Celebrex, the leader of the cox-2 crowd, is what the drug companies like to call a blockbuster—earning Pharmacia more than $1.5 billion annually since it came on the market in 1999, and raking in more than $3 billion last year. Also hanging directly on the verdict is an additional, and almost as large, revenue stream from another cox-2 blockbuster called Vioxx, manufactured by Merck.

In his surprising decision, Judge David G. Larimer of the federal district court in western New York invalidated the University of Rochester's patent on cox-2 inhibitors, ruling that the university patent is too broad and nonspecific to be considered a full-fledged invention. Larimer's decision hinges largely on the fact that the University of Rochester scientists never took what he calls the "last, critical step" of actually isolating a drug compound themselves.

Larimer's ruling gives me a massive headache. At first blush, it is exactly what I have repeatedly called for. Larimer's decision reminds us that a patent "must be sufficiently concrete so that it can be described for the world to appreciate the specific nature of the work that sets it apart from what was before." The notion sounds obvious. But it has been almost entirely absent in the Wild West of intellectual-property claims in recent years. The patent office has handed out scores of vague, broad claims to entire areas, from instant messaging to human gene therapy.

But on closer inspection, the judge has it wrong. If our system is designed to reward innovation, we need to fairly consider the seminal research that makes an invention possible. If Larimer's decision holds up, not only would it threaten the validity of countless dubiously broad patents (a good thing), it would also lead to a patent system that is fundamentally incompatible with the kind of basic research that universities do.

Let's take a moment to consider what the University of Rochester researchers accomplished. The story begins back in the 1960s, when Rochester biochemist Donald Young studied an enzyme called cyclooxygenase, or "cox," whose activity is blocked by aspirin and other anti-inflammatory drugs. Young's research led him to distinguish between two distinct parts of the enzyme that he came to dub cox-1 and cox-2.

Further study of cox-1 showed that it does not even play a role in inflammation itself but rather, among other things, regulates the secretion of gastric acid in the stomach. In the distinction between the functions of cox-1 and cox-2, the team recognized a potential gold mine: they might be able to directly target cox-2, thereby suppressing pain and inflammation without causing stomach irritation, the bane of all previous painkillers—from aspirin to ibuprofen—that act on the cox enzyme.

Simply discovering cox-2 was an important contribution to the field. But the researchers didn't stop there. By the early 1990s, Young's team identified the gene in humans that is responsible for producing cox-2 and discovered how it causes inflammation within individual cells. The group even developed a method for testing to see whether given compounds might selectively inhibit cox-2 in humans.

A judge's decision on who invented a common painkiller seems like an antidote to overly broad patents. But in fact, it devalues the basic university research that makes such key inventions possible.

No matter how you look at it, in other words, there is little question that the pioneering University of Rochester work paved the way for a new generation of painkillers that would be easy on the stomach. And in 2000—after eight years—the U.S. Patent Office granted the Rochester team a broad patent covering a "method" for selectively inhibiting cox-2.

What's really at issue in this case is whether our patent system can reasonably be made to account for seminal research contributions like the one made by Young and his team. It is not a simple question. Sure, the university researchers didn't do the costly drug development or the clinical testing required to bring Celebrex and Vioxx to market. And narrow and specific patent claims tend rightly to reward those who assume precisely those kinds of laborious and costly roles.

But universities are not in the drug development business. In this case, there seems to be little doubt that Celebrex and Vioxx are on the market today only because of the pathbreaking contribution made by the Rochester researchers. The university has already announced that it will appeal the decision; this will be a critical intellectual-property case to watch. Judge Larimer opined that a broad and nonspecific patent claim is little more than "an attempt to preempt the future before it has arrived." I'm so strongly in agreement with that sentiment that it is echoed in the very name of this column. But we need a patent system that distinguishes between those who would "preempt" the future and those who actually help create it. TR

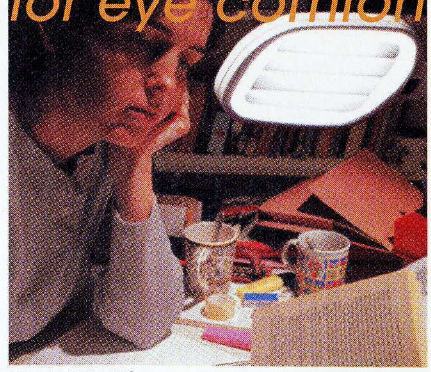
INDEX

PEOPLE AND ORGANIZATIONS MENTIONED IN THIS ISSUE

PEOPLE

ORGANIZATIONS

Lighting Technology for eye comfort


The VERILUX® HappyEyes® Floor Lamp will change the way you see and feel about your living or work spaces.

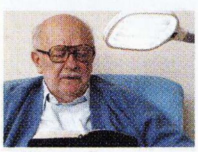
A floor lamp that spreads sunshine all over a room

The VERILUX® HappyEyes® Floor Lamp brings many of the benefits of natural daylight indoors for glare-free lighting that's perfect for a variety of indoor activities.

Ever since the first human went into a dark cave and built a fire, people have realized the importance of proper indoor lighting. Unfortunately, since Edison invented the light bulb, lighting technology has remained relatively prehistoric. Modern light fixtures do little to combat many symptoms of improper lighting, such as eyestrain, dryness or burning. As more and more of us spend longer hours in front of a computer monitor, the results are compounded. And the effects of indoor lighting are not necessarily limited to physical well being. Many people believe that the quantity and quality of light can play a part in one's mood and work performance. Now VERILUX®, a leader in healthy lighting since 1956 has developed a better way to bring the positive benefits of natural sunlight indoors.

Use the VERILUX® HappyEyes® Floor Lamp...


...for hobbies...


...for reading...


...for working...


...and when you need a good source of light for close-up tasks.

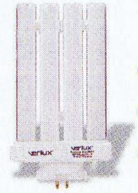
The VERILUX® HappyEyes® Floor Lamp will change the way you see and feel about your living or work spaces. Studies show that sunshine can lift your mood and your energy levels, but as we all know the sun, unfortunately, does not always shine. So to bring the benefits of natural daylight indoors, VERILUX, The Healthy Lighting Company™, created the VERILUX HappyEyes Floor Lamp that simulates the balanced spectrum of daylight. You will see with more comfort and ease as this lamp provides sharp visibility for close tasks and reduces eyestrain.

Verilux®

You don't need the Sun to get many of the natural benefits of daylight

- Replicates the balanced spectrum of natural sunlight
- See with comfort and ease
- Creates natural, glare-free light
- Provides sharp visibility
- Uplifting, cheerful and bright
- Flexible gooseneck design
- Instant-on, flicker-free light

Technology revolutionizes the light bulb



- 5,000 hours bulb life
- Energy efficient
- Shows true colors

Its 27-watt compact fluorescent bulb is the equivalent to a 150-watt ordinary light bulb. This makes it perfect for activities such as reading, writing, sewing and needlepoint, and especially for aging eyes. For artists, the VERILUX HappyEyes Floor Lamp can bring a source of natural light into a studio, and show the true colors of a work. This lamp has a flexible gooseneck design for maximum efficiency, and an "Instant On" switch that is flicker-free. The high fidelity electronics, ergonomically correct design, and bulb that lasts five times longer than an ordinary bulb make this product a must-see.

This light can change the way you live and work

"I love it! Reading is so much easier on my eyes. It's also great for doing crafts. The lamp's light weight allows me to bring it anywhere.
—Karen R. CA

It really brightens up my office, Thank you.
—Jan L. GA

I use my computer all the time and WOW what a difference. I just put it up and I can see!
—Kathy N. CA

It is really nice and eliminates the glare!
—Nita P. CA

It is a nice sunny product for a windowless office."
—Edith L. NJ

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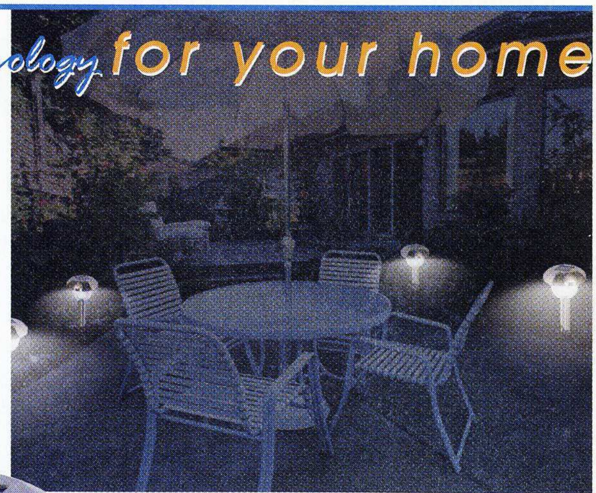
Lighting Technology **for your home**

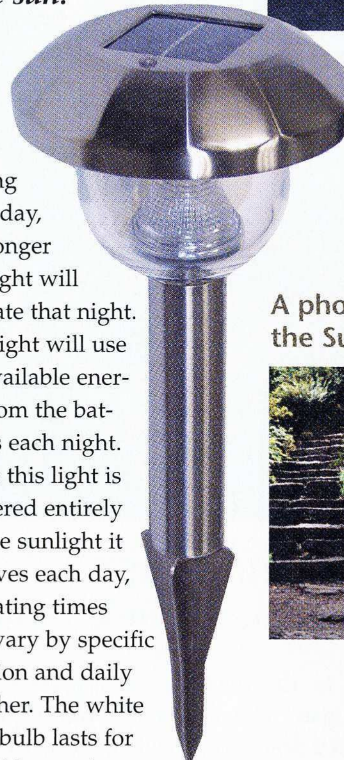


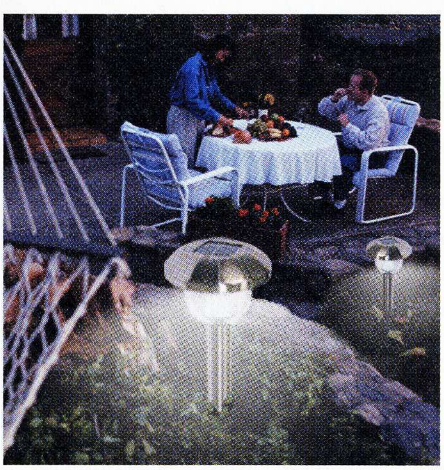
Harness the power of the sun with elegant stainless steel solar lights

The Sun-Glow® Solar Light illuminates patios, gardens and walkways, and draws its power from the sun.

If you're like most of us, you've probably spent a considerable amount of time making your home and yard look beautiful. From maintaining your lawn to planting gardens and even the arduous task of mulching, the way your yard looks is important. Now you can add a bit of class to your landscaping efforts with the Sun-Glow® Solar Light. The Sun-Glow® Solar Light graces any patio, garden, walkway or driveway and illuminates them, adding a touch of elegance to your home. With its clear glass lens it uses Solar energy to power and charge the built-in NiCad batteries during the day and turns its photo-cell LED light "ON" automatically at dusk, day after day, night after night.

Put your good taste in the spotlight. The Sun-Glow® Solar Light has a solar cell that converts sunlight into electricity. This electricity is used to recharge the built-in batteries each day. A photo-cell sensor automatically turns on the light at night. The more sunlight received during each day, the longer the light will operate that night. The light will use all available energy from the batteries each night. Since this light is powered entirely by the sunlight it receives each day, operating times will vary by specific location and daily weather. The white LED bulb lasts for 10,000 hours, is incredibly bright and will never need to be replaced. On a full charge (six to eight hours in full sunlight), this light will last for eight to 15 hours at night.





There are no wires to install, allowing easy placement anywhere on your lawn or pathways. The white LED bulb is incredibly bright, and will never need to be replaced.

Place these attractive lights all around your house. Let's be honest, lights for your home are practical, especially in the dark. But sometimes the lights you place along your driveway, or walkway can be unattractive. This light eliminates that problem by combining practicality with class and gives you the kind of accents you've been looking for. The Sun-Glow® Solar Light is perfect for outdoor parties, or simply when you come home at night, and you can't easily find your way up the path. There are no wires to install, allowing easy placement anywhere on your lawn. Made with real stainless steel, this solar light will make a beautiful addition to any house. Above ground height measures 11 inches.

- *Stainless Steel and prismatic construction*
- *Power-efficient single-crystalline solar cell*
- *New technology bright white LED bulb*
- *Light will last for eight to 15 hours when fully charged*
- *Some assembly required*

A photo-cell sensor automatically turns on the Sun-Glow® Solar Lights at night.

Try it yourself for 30 days! Impress your friends and neighbors with these elegant lights. Liven up the party, or even just enjoy them yourself when you relax at night. The Sun-Glow® Solar Light is backed by TechnoScout's exclusive in-home 30-day trial. If you aren't completely satisfied, simply return it for the full purchase price, less shipping and handling.

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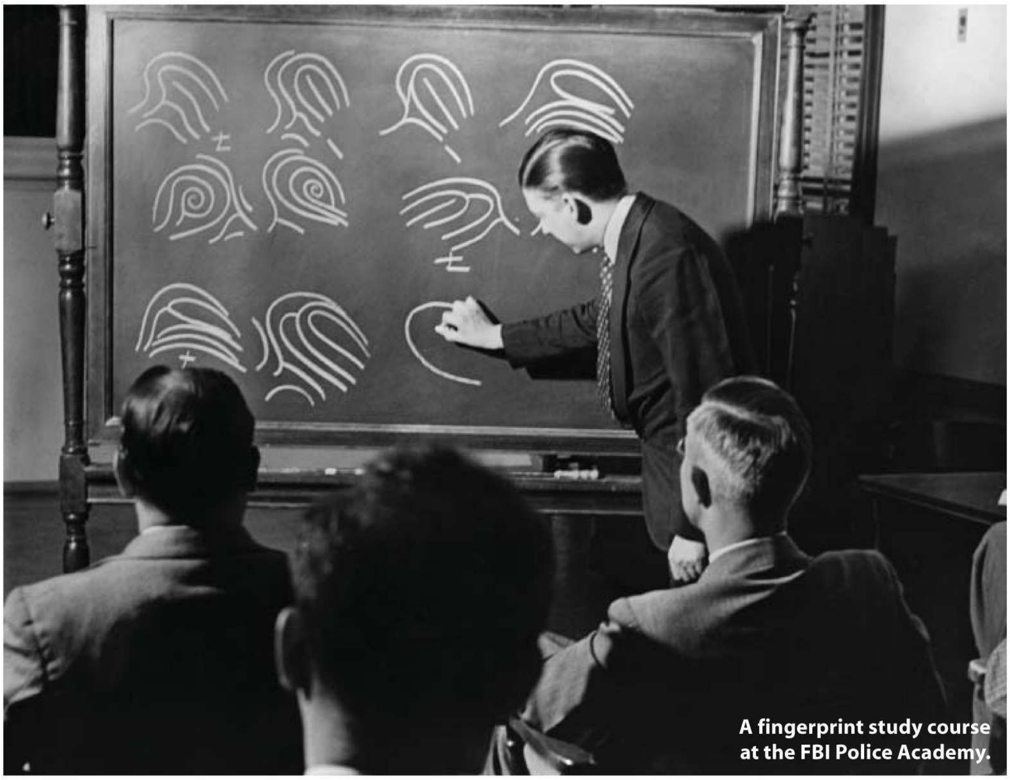

A fingerprint study course at the FBI Police Academy.

COURTESY OF CORBIS

FINGERPRINTING'S FINGER-POINTING PAST

A bitter battle between two Brits launched forensic science

While face recognition software, iris scanning, and other identification technologies have been capturing headlines as promising new authentication and security tools, fingerprint records, arguably the first biometric databases, go back more than a hundred years. The idea of using fingerprints for identification was startlingly novel in its time—and caused a bitter dispute between two men who claimed to have invented the technology.

During the 1870s, Henry Faulds, a Scottish missionary working as a doctor in Japan, happened across an ancient pot marked with its creator's fingerprints. The discovery inspired him to investigate fingerprints. In 1880, Faulds published a letter in *Nature* in which he observed that "when bloody finger-marks or impressions on clay, glass, etc., exist, they may lead to the scientific identification of criminals." The next month, *Nature* published a reply from William Herschel, an India-based British magistrate. Herschel had collected fingerprints since the 1860s and suspected that each person's fingerprint was unique—but he had never studied their potential for forensic use.

Neither letter received much attention until 1892, when Francis Galton, Charles Darwin's cousin and a noted scientist himself, published *Finger Prints*. Galton established that fingerprints are unique and don't change over a person's lifetime, and suggested a classifying system. In 1901, Scotland Yard founded its Fingerprint Bureau, based largely on Galton's system. Although Faulds had suggested a similar system to Scotland Yard years earlier, Galton and Herschel took credit for the innovation. Infuriated, Faulds instigated a public battle of letters with Herschel that would last until his rival's death in 1917.

Regardless of who originally envisioned fingerprints as a forensic tool, the practice took off. In 1902, fingerprints were first used as evidence in a British court to identify a burglar who had stolen some billiard balls. And 1902 was also the year that fingerprints were first systematically employed in the United States, when the New York Civil Service Commission began fingerprinting applicants to prevent them from cheating on tests.

Although fingerprinting may recall the Sherlock Holmesian era during which it was created, new tools have brought the system into the digital age. Today, the FBI's fingerprint system contains more than 40 million people's fingerprints. A suspect's prints can be identified within two hours; just a few years ago, the process could take weeks. —*Lisa Scanlon*

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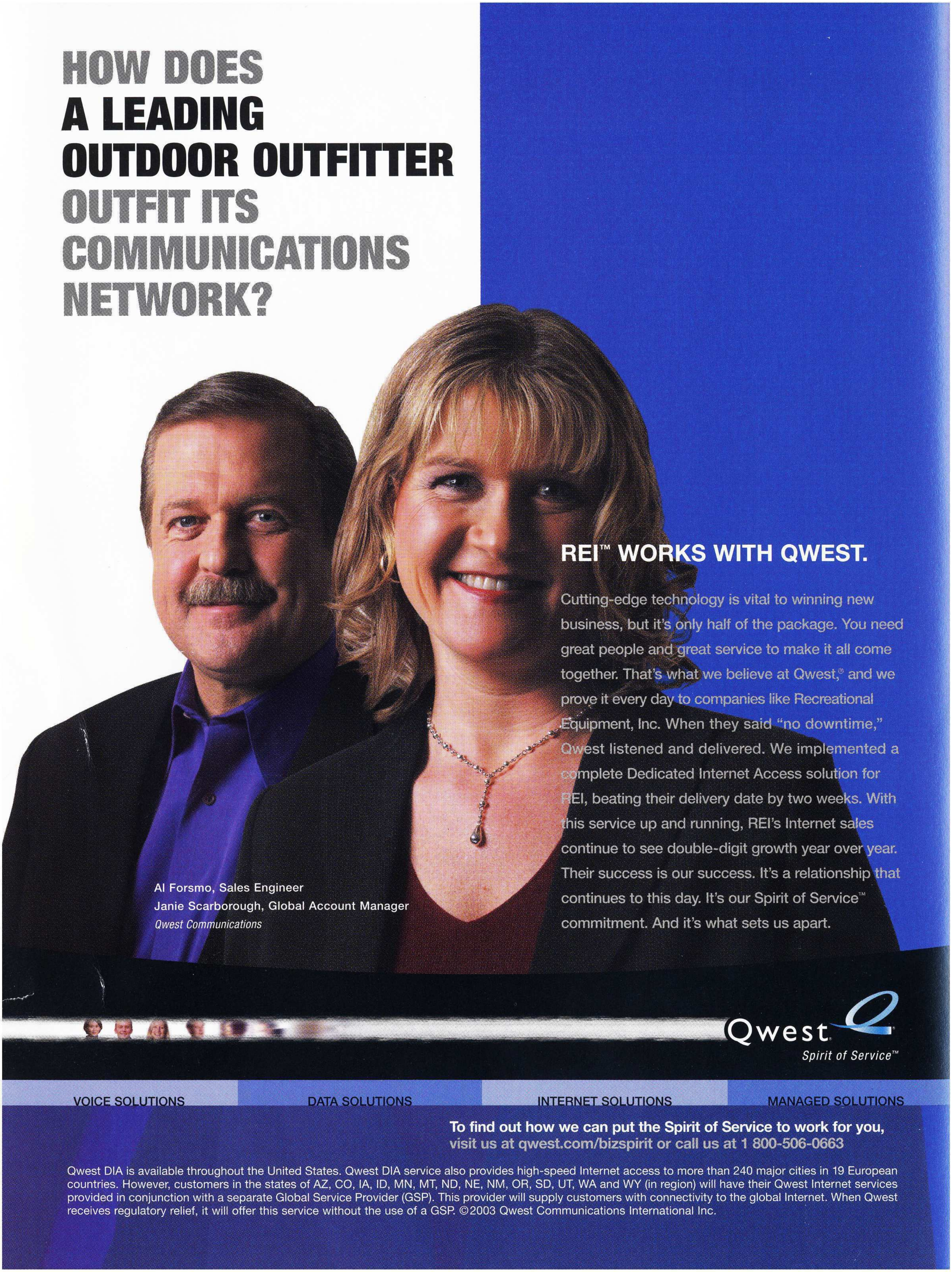
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